

## SUPPLEMENTARY MATERIAL

### **Molecular insights into titin's A-band**

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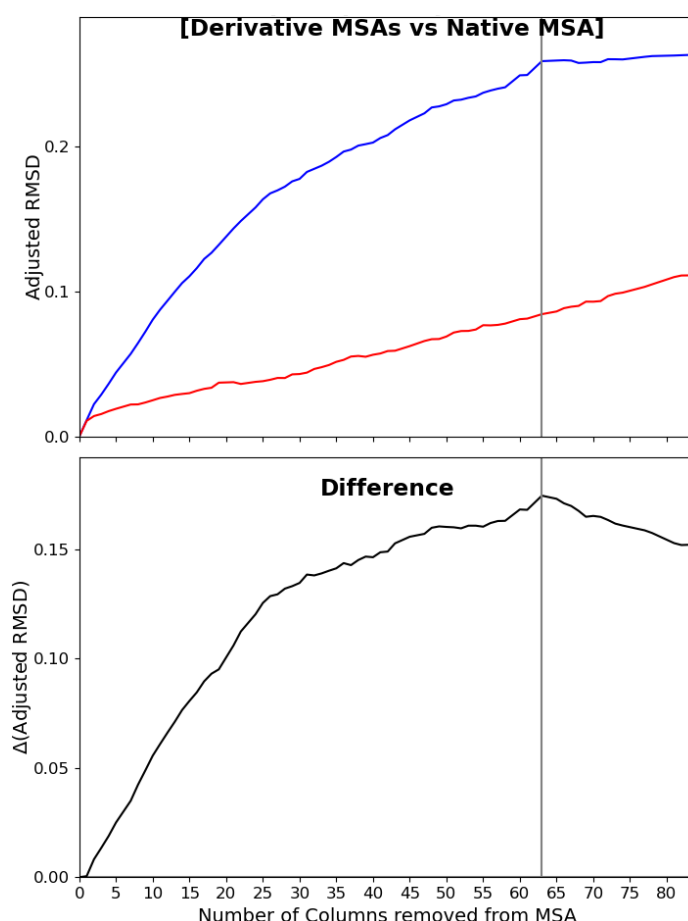
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**Fig S1: Global MSA alignment of FnIII domains from titin's A-band showing consensus residues.** For each position, the SoP (sum-of-pairs) score is given, where the higher the score the greater the consensus for that alignment position. SoP scores  $>0.5$  (see FigS2) and were taken to constitute the global conservation consensus for A-band FnIII domains and are marked in pale blue.

|        |             |               |     |                                 |                                         |     |                 |           |                             |                                       |                                 |                                 |                               |                                 |
|--------|-------------|---------------|-----|---------------------------------|-----------------------------------------|-----|-----------------|-----------|-----------------------------|---------------------------------------|---------------------------------|---------------------------------|-------------------------------|---------------------------------|
| A2.1   | G L P G P C | K D I K       | ... | A S D I T K S S C K L T W E P F | I D G G S P I I N V Y V E R             | ... | E A G R         | - R T     | - Y P Y P                   | - M S                                 | ...                             | G E N K L S W T V K D L I P N   | - G E Y F F R V K A V N K V G | - G E Y F I E L N K P V I A Q   |
| A9.1   | D V P G P P | K D I K       | ... | P V T N R K M C L L N W S D     | F E D D G G S E I T G L Y I E R K       | ... | D A K M         | - H T     | - W R Q P                   | ...                                   | ...                             | I E T E R S K R I A K N K F     | - G C P P P V E I             | - G P I L V A L                 |
| A16.1  | D V P G P P | K D I K       | ... | V S D I T R G S C R L S W K M   | P D D G G S D R I K G V Y I E R K       | ... | T I D G         | - K A     | - W T K V                   | - N P                                 | ...                             | D C G S T T F V V P D L I S E   | - Q Q Y F F R V R A E N R F G | - I G P P P V E T I Q R T T A R |
| A23.1  | D V P G P P | G T P F L     | ... | A H L I T K S E C K L T W P F   | P E D D G G S P I T N V Y I E R K       | ... | E S D R         | - R A     | - W T P V                   | - T Y                                 | ...                             | T V T R N A T V Q G L I Q G     | - K A Y F F R I A E A N S I G | - M P P P V E T S A L V I R     |
| A30.1  | D K P G P P | R D I E       | ... | V S E I R K D S C Y L T W K E   | P L D D G G S I T N V Y V E R           | ... | D V A S         | - A Q     | - W S P L                   | - S A                                 | ...                             | T S K K S H F A K H L N E G     | - N Q Y I F R V A E A N S I G | - R G P P V E T P K P I K A L   |
| A37.1  | D R P G P C | Q N I K       | ... | V T N V T K E N C T I S W E N P | L D N G G S E I T N F I V E Y R         | ... | K P N Q         | - K G     | - W S I V                   | - A S                                 | ...                             | D V T K R L I K A - N L I A N   | - N E Y F F R V C A E N K V G | - V G P T I E T K T P I L A I   |
| A44.1  | D T P G P P | S D I K       | ... | V S D V T K S C H V S W A P P   | E N D G G S Q V T H Y I V E R K         | ... | E A D R         | - K T     | - W S T V                   | - T P                                 | ...                             | E V K K T S F H V T N L V P G   | - N E Y F F R V T A V N E Y G | - P G V P T V P K P V L A S     |
| A55.1  | D T P G P P | I N V T       | ... | V S I S K D S A V Y T W P P I   | I D G G S P I I N V Y I E R K           | ... | D A E R         | - E S     | - W S T V                   | - T T                                 | ...                             | E C S T S F R V N L I E G       | - N E Y F F R V A E N E Y G   | - I E D P G P T R D A V K       |
| A66.1  | D T P G P P | L N I R       | ... | P T D I T K D S V T L H W D L P | I D G G S R I T N Y I V E R K           | ... | E A T R         | - K S     | - Y S T A                   | - T T                                 | ...                             | K C H K C T Y K V T G L S E G   | - C E Y F F R V M A E N E Y G | - I E G P T T E T P V K A S     |
| A72.1  | D T P G P P | Q D I K       | ... | K E V E T K S V T L T W D P P   | L D G G S K I N Y I V E R K             | ... | E S T R         | - K A     | - Y S T V                   | - A T                                 | ...                             | N C H K T S W K V Q L Q L E G   | - C S Y F F R V L A E N E Y G | - I G L P A E T A S V K K A S   |
| A80.1  | D T P G P P | V D V E       | ... | V T I T K D S V S I T W P P I   | I D G G S P I I N V Y I E R K           | ... | D A E R         | - E S     | - W S T V                   | - T T                                 | ...                             | E C S T S F R V N L I E G       | - N E Y F F R V A E N E Y G   | - I E D P G P T R D A V K       |
| A90.1  | D T P G P P | Q N I A       | ... | K E V E R K D S A F L W E P P   | I D G G A K V K N Y V I D K R           | ... | E S T R         | - K A     | - Y A N V                   | - S S                                 | ...                             | K C S K T S F R V E N L T E G   | - A I Y F F R V M A E N E Y G | - V G V P V T V D A V K A A     |
| A99.1  | D S P A P P | V N I T       | ... | I R E V K D S V T I S W E P P   | I D G G A K I T N Y I V E R K           | ... | E T T R         | - K A     | - Y A T I                   | - T N                                 | ...                             | N C T K T T F R I E N L Q E G   | - C S Y F F R V L A S N E Y G | - I G L P A E T T E P V K K A   |
| A121.1 | D T P G P P | T N I T       | ... | V Q D V T K E S A V I S W D P   | E N D G G A P K N Y H I E R K           | ... | E A S K         | - K A     | - W V S V                   | - T N                                 | ...                             | N C N R L S Y K V N L Q E G     | - A I Y F F R V S E N E Y G   | - V G I P A E T K E G V K I T   |
| A132.1 | D T P G P P | R D I E       | ... | H V D V D K T E S V L W M K P   | P D D G G S P I T G V L Y E Y Q         | ... | E E G T         | - Q D     | - W I K E                   | - K T                                 | ...                             | V T N I L E C V V T G L Q Q G   | - K T Y F F R V K A E N I V G | - L G L P - D T T I P I E Q C   |
| A143.1 | D T P G P P | G P I T       | ... | K D V T R G S A T L M W D A P   | L D G G A R I H Y V V E R K             | ... | E A S R         | - R S     | - W Q V I                   | - S E                                 | ...                             | K C T R Q I F K V N D L A E G   | - V P Y F F R V S A V N E Y G | - V G E P P E P P I V A T       |
| A154.1 | D T P G P C | P S V K       | ... | K E V E S R D S V T I T W E I P | I D G G A P I N N Y I V E R K           | ... | E A A M         | - R A     | - F K T V                   | - T T                                 | ...                             | K C S K T L Y R I S G L V E G   | - T M H Y F R V L P E N I Y G | - I E G P C E T S D A V L V S   |
| A15.1  | D P G P P   | V D V E       | ... | V T I T K D S V S I T W P P I   | I D G G S P I I N V Y I E R K           | ... | D A E R         | - E S     | - W S T V                   | - T T                                 | ...                             | E C S T S F R V N L I E G       | - N E Y F F R V A E N E Y G   | - I E D P G P T R D A V K       |
| A10.2  | D L G P P P | T S P E R L T | ... | Y T E R Q R S T I T L D W K E   | P R S N G S P I Q G Y I E R K           | ... | R H D K         | - P D     | - F E R V                   | - N K                                 | ...                             | R L C P T T S F L V E N L D E H | - Q M Y F F R V K A V N E I G | - E S E P S I T N L N V I Q D   |
| A17.2  | Y P P D P P | I K L K       | ... | I G L I T K N T V H L S W K P   | P D D G G S P V T H Y I V E C L A W P T | ... | G T K K         | - E A     | - F R V Q                   | - N K                                 | ...                             | R D V E E L Q F T V E D L V E G | - G E Y F F R V A A N A A G   | - V S K P S A T V G P C D C Q   |
| A24.2  | V T P P P P | E D L E       | ... | K E V E T K S V T L T W M P P   | K Y D G G S E I I N V L Y E R K         | ... | L I D T         | - E K     | - F H K V                   | - T N                                 | ...                             | D N L S R K Y T V K G L K E G   | - C S Y F F R V S A V N I V G | - Q G K P S F T C P R I V A K   |
| A31.2  | H P P G P P | R D I E       | ... | H V D V D K T E S V L W M K P   | P D D G G S P I T G V L Y E Y Q         | ... | E E G T         | - Q D     | - W I K E                   | - K T                                 | ...                             | V T N I L E C V V T G L Q Q G   | - K T Y F F R V K A E N I V G | - L G L P - D T T I P I E Q C   |
| A38.2  | D R P G P P | E N I H       | ... | I A D K G K T F V Y L K W R R P | D Y D G G S P I S Y H V E R R           | ... | L K G S         | - D D     | - W E R V                   | - H K                                 | ...                             | G S I K E T H Y M V D R C V E N | - Q I Y E F R V Q T K N E G G | - E S D W K T E E V V V K E     |
| A45.2  | S E P D P P | R K L E       | ... | A T E M T K N S A T L A W P L P | I D G G A K I D G V Y I S Y R           | ... | E E E Q A D P R | - D T     | - W E R V                   | - S V                                 | ...                             | V K D I S L V V T G L K E G     | - K K Y F F R V A A N A A G   | - V S L P R E A E G V Y E A K   |
| A56.2  | Q T P G P P | V D I K       | ... | V R S V S K S C S I G W K K P   | H S D G G S R I I G V Y V D F L         | ... | T E E N K       | - T       | - W Q R V                   | - M K                                 | ...                             | S L S I Q Y S A D L T E G       | - K E Y F F R V S A E N E G   | - E G T P S E I - T V V A R     |
| A67.2  | E A P S P P | D S L N       | ... | I M D I T K S V S L A W P K     | K H D G G S K I T G V Y I E A Q         | ... | R K G S         | - D Q     | - W T H I                   | - T T                                 | ...                             | V K G L E C V V R N L T E G     | - E E Y T F Q V M A N S A G   | - R S A P E S - R P V I V K     |
| A78.2  | E R L P P P | G K I T       | ... | L M D V T R N S V S L A W P K   | H D G G S R I L G V Y I E M Q           | ... | T K G S         | - D K     | - W A T C                   | - A T                                 | ...                             | K V E T E A T I T G L I Q G     | - E E Y S F R V S A Q N E K G | - I S D P R Q L S V P V I A Q   |
| A89.2  | E V P G P P | G K I T       | ... | V D D V T R N S V S L A W P K   | H D G G S R I I Q V Y I E M Q           | ... | A K H S         | - E K     | - W S E C                   | - A R                                 | ...                             | K S Q A V Y I T N L T Q G       | - E E Y F F R V V A E N E Y G | - R S D P R S L A V P I V A K   |
| A100.2 | E P P P P   | G K V T       | ... | V T D S Q T S A S I L W K E P   | H D G G S I T N Y I V E R K             | ... | P K G T         | - E R     | - W M W V                   | - A E                                 | ...                             | S V K E R A V Y W K L I P N     | - Q E Y F F R V A E N E Y G   | - K S D P R L S V P V I A K     |
| A111.2 | E P L P P P | G R V T       | ... | L V D V T R N T A T I K W E P   | P E S D G G S K I T G V Y I E M Q       | ... | T K G S         | - E K     | - W S T C                   | - T Q                                 | ...                             | V K T L E A T I S G L T A G     | - E E Y F F R V A A V N E K G | - R S D P R Q L G V P V I A K   |
| A122.2 | E K P S P P | E K L G       | ... | V T S I S K D S V T L W L K P   | H D G G S R I I V H Y V E A L           | ... | E K Q G         | - K N     | - W K V C                   | - A V                                 | ...                             | A K S T H H V S G L R E N       | - S E Y F F R V I A E N A G   | - L S D P R E L L P V L I K     |
| A133.2 | E V P P P P | R D I E       | ... | V S E I R K D S C Y L T W K E   | P L D D G G S I T N V Y V E R           | ... | D V A S         | - A Q     | - W S P L                   | - S A                                 | ...                             | T S K K S H F A K H L N E G     | - N Q Y I F R V A E A N S I G | - R G P P V E T P K P I K A L   |
| A144.2 | E Q A P P P | R R I D       | ... | V D D T S S A V A L W K P       | H D G G S R I T G Y L L E M R           | ... | Q K G S         | - D L     | - W E A G                   | - G H                                 | ...                             | T K Q L T F T V E R L V E K     | - S E Y F F R V K A K N D A G | - Y S P E R A F S S V I V K     |
| A155.2 | E V P L V P | A K L E       | ... | V D V D T K S V T L A W E K P   | I D G G S R I T G V Y L E A C           | ... | K A G T         | - E R     | - W M K V                   | - V T                                 | ...                             | L K P T V L E H T V T S L N E G | - E Q Y F F R I R A Q N E K G | - V S E P P E R T V A T V Y Q   |
| A5.3   | D P G P P   | I N F V       | ... | F E D I R K T S V L C K W E P   | P L D D G G S E I I N T Y I E R K       | ... | D K T K P D S E | - V I W V | - T T                       | ...                                   | T L H K C K Y S V T K L I E G G | - P E Y F F R V R A E N R F G   | - P E P P C V S - P L V A K   |                                 |
| A12.3  | D R P G P P | R N I A       | ... | V T D I K A E S C Y L T W D A P | L D G G S I T N Y I V E R K             | ... | D A E R         | - E S     | - W S T V                   | - T T                                 | ...                             | E C S T S F R V N L I E G       | - N E Y F F R V A E N E Y G   | - I E D P G P T R D A V K       |
| A19.3  | D H P G P P | V G P I K     | ... | F E S V S A D Q M T I S W P P   | K D D G G S K I T N Y I E R K           | ... | E A N R         | - K T     | - W V H V                   | - S S                                 | ...                             | E P K E C T Y T I P K L L E G   | - H E Y F F R I M A Q N K Y G | - I E P I D L S - E P E T A R   |
| A26.3  | D H P G P P | V G P M S     | ... | F D E V T K D Y M V I S W K P   | P L D D G G S K I T N Y I E R K         | ... | E V G K         | - D V     | - W M P V                   | - T S                                 | ...                             | A S A K T T C K V S K L L E G   | - K D Y I F R I A E N L Y G   | - I S D P L S - D S M A K K     |
| A33.3  | D V P G P P | T G P I N     | ... | I L D V T P E H M T I S W A P P | K D D G S P I I N V Y I E R K           | ... | D T R K         | - T T     | - W G V V                   | - S S                                 | ...                             | G S K T L K I P H L Q G         | - C E Y F F R V A E N E Y G   | - I E D P G P T R D A V K       |
| A40.3  | D K P G P P | R N I K       | ... | I D V D S D R C T V C W D P     | P E D D G G C E I Q N Y I L E K C       | ... | E T R K         | - M V     | - W S T Y                   | - S A                                 | ...                             | T V I T P G T V T R L I E G     | - N E Y F F R V R A E N I G   | - T G P P T S - K P V I A K     |
| A47.3  | D A P G P P | P D P F D     | ... | I S D I D A C S L S W H I P     | E D D G G S I T N Y I V E K C           | ... | D V S R         | - G D     | - W V T A                   | - L A                                 | ...                             | S V T K T S C R V K L L I P G   | - Q E Y F F R V R A E N R F G | - I E P I T S - P K M V A Q     |
| A58.3  | K S P G P P | G T P I K     | ... | V E T V T A E A M T L W M P P   | P D D G G S E I T N Y I E R K           | ... | D V N V         | - N K     | - E A E E                   | - A E                                 | ...                             | A V G S G R V A T K L I E G     | - H E Y F F R V A E N E Y G   | - V E G I C T T E P V A K       |
| A69.3  | D P G P P   | T G P I K     | ... | D E V S S D P F T E S W D P     | P E N D G G S P I N V Y I E M R         | ... | D T D T         | - T T     | - W V E L                   | - S T                                 | ...                             | T V I R T Y K A T L T T G       | - L E Y F F R V A A N E Y G   | - V E G I C T T E P V A K       |
| A80.3  | D K P G P P | T G P V K     | ... | M D E V T A D S I T S W G P P   | K Y D G G S I N N Y I V E R K           | ... | D T S T         | - T T     | - W Q I V                   | - S A                                 | ...                             | T V A R T T I A C A R L K T G   | - Q E Y F F R I A E N R F G   | - K S T Y L N S - E P T V A Q   |
| A91.3  | D K P G P P | G P V K       | ... | P D D V S A E S I S W M P P     | L Y T G G C Q I S N Y I V A K R         | ... | D T T T         | - T V     | - W D V V                   | - S A                                 | ...                             | T V A R T T L K V T L K T G     | - T E Y F F R I A E N R F G   | - Q S F A L S - D P I V A K     |
| A102.3 | E K P G P P | V G P V R     | ... | F D E V T K D Y M V I S W K P   | P L D D G G S K I T N Y I E R K         | ... | D T R K         | - T T     | - W G V V                   | - S S                                 | ...                             | G S K T L K I P H L Q G         | - C E Y F F R V A E N E Y G   | - I E D P G P T R D A V K       |
| A113.3 | D R P G P P | G P I R       | ... | I D E V S C D S I T S W M P P   | P Y D G G C Q I S N Y I V E K K         | ... | E T T S         | - T T     | - W H I V                   | - S Q                                 | ...                             | A V A R T S I K I V R L T T G   | - S E Y F F R V C A E N R Y G | - K S Y S E S - S A V A E       |
| A124.3 | D P G P P   | T G P V M     | ... | I S D I T E S V T K W E P P     | P L D D G G S Q V T N Y I L K R         | ... | E T S T         | - A V     | - W T E V                   | - S A                                 | ...                             | T V A R T M M K V M L T T G     | - Q E Y F F R I A E N R F G   | - I S D H I D S - A C T V T A Q |
| A135.3 | G P P P P   | V G P I K     | ... | V T D S Q T S A S I L W K E P   | H D G G S I T N Y I V E R K             | ... | P K G T         | - E R     | - W M W V                   | - A E                                 | ...                             | S V K E R A V Y W K L I P N     | - Q E Y F F R V A E N E Y G   | - K S D P R L S V P V I A K     |
| A146.3 | G R P G P P | V T G P I E   | ... | V S S V A E S C V L S W G P     | K D D G G T E I T N Y I V E R K         | ... | E S G T         | - T A     | - V Q L V                   | - N S                                 | ...                             | S V K R T Q I K V T H L T K Y   | - M E Y S F R V S E N R F G   | - V S K P L S - A P I A E       |
| A157.3 | D K P G P P | T G P I K     | ... | I D E I D A T S I T I S W E P P | L D D G G A P I S G V Y E Q R           | ... | D A H R         | - P G     | - W L P V                   | - S E                                 | ...                             | S V T R S T F K F T R L T E G   | - N E Y F F R V A A N R F G   | - I G S Y L V S - E I E C R     |
| A51.3  | D K P G P P | A S V K       | ... | I N E M Y S D R A M I S W E P P | L D D G G S E I T N Y I V D K R         | ... | E T S R         | - P N     | - W L V Q                   | - S A                                 | ...                             | T V P I T S C S V E K L I E G   | - N E Y F F R I C A L N K Y G | - V D D P V T - E P I A K       |
| A62.3  | D V P G P P | G P V T       | ... | I S N V S A E K A T I T W P P   | L E D D G S P I K S Y I L E R K         | ... | E T S R         | - L       | - W T V E                   | - S E                                 | ...                             | D I O S C R H V A T K I Q G     | - N E Y F F R V A E N E Y G   | - K E G P Q S - E P V A K       |
| A73.3  | D R P G P P | E P G I A     | ... | V T E V T S E K C V L S W P P   | L D D G G A K I D H Y I V A K R         | ... | E T S R         | - L A     | - W T N V                   | - A S                                 | ...                             | E Q V G T K L V K T L K L G     | - N E Y F F R V M A N K Y G   | - V G E P L S - E P V L A V     |
| A84.3  | D R P G P P | G P V M       | ... | I S G V T A E K C T L A W P P   | L D D G G S I T N Y I V E R K           | ... | E T S R         | - L V     | - W T V V                   | - D A                                 | ...                             | N Q V T I S C K V T K L L E G   | - N E Y F F R I M A V N K Y G | - V G E P L S - E P V A K       |
| A95.3  | D R P G P P | G P V Q       | ... | V T N I T E K M T L W D A P     | L D N G G A P I S H Y I V E R K         | ... | E T S R         | - L A     | - W A E D                   | - E D                                 | ...                             | K C E A Q S Y T A I K L I G     | - N E Y F F R V A A N E Y G   | - V G R L D S - D P V A K       |
| A106.3 | D R P G P P | E P G I K     | ... | V T G V T A E K C V L A W M P P | L D D G G A N I S H Y I V A K R         | ... | E T S R         | - L S     | - W T Q V                   | - S T                                 | ...                             | E Q A L N Y K V T L K L G       | - N E Y F F R V M A N K Y G   | - I E P L S - G P V T A K       |
| A117.3 | D K P G P P | A P G I E     | ... | I N G L T A E K C S L S W G P   | P Q E D G G A D I D Y Y H R K R         | ... | E T S H         | - L A     | - W T I C                   | - E G                                 | ...                             | E L Q M T S C K V T K L L P G   | - N E Y F F R V T V K N Y G   | - V G E P L S - V A I K A L     |
| A128.3 | D K P G P P | G P I E       | ... | F K V T A E K I T L W P P       | P A D D G G A K A I T H Y I E R K       | ... | E T S R         | - V V     | - W S M V                   | - S E                                 | ...                             | H L E E C I I T T T K I I K     | - N E Y F F R V A A N K Y G   | - I E P L S - D S V A K         |
| A139.3 | D T P G P P | V G P I R     | ... | V T N I T E K M T L W D A P     | L D N G G A P I S H Y I V E R K         | ... | E T S R         | - L A     | - W A E D                   | - E D                                 | ...                             | K C E A Q S Y T A I K L I G     | - N E Y F F R V A A N E Y G   | - V G R L D S - D P V A K       |
| A150.3 | D S P G C P | G K I T       | ... | F K S V T A E K C T L A W S P   | L Q E D G G A E I T H Y I V E R         | ... | E T S R         | - L N     | - W V I V                   | - E G                                 | ...                             | E C P T L S Y V T V T L I K N   | - N E Y F F R V A A N K Y G   | - P G P P V S - E P I V A R     |
| A161.3 | G P S N S P | E P G I E     | ... | Y D D I Q V R S V S W R P P     | A D D G G A D I L G Y I L E R R         | ... | E V P K         | - A A     | - W Y T I                   | - D S                                 | ...                             | R V R G T S L V V G K L E N     | - N E Y F F R V S A E N A G   | - I S K P L K S E E P V T P K   |
| A6.3   | F P P G P P | G P I K       | ... | V S D V T S E M L S W E P P     | D N G S P I L G Y V I E R K             | ... | E T S R         | - L       | - W T V E                   | - S E                                 | ...                             | D I O S C R H V A T K I Q G     | - N E Y F F R V A E N E Y G   | - K E G P Q S - E P V A K       |
| A17.3  | R L P G P P | G K P K       | ... | V L A R T K S M V S W P P       | P L D N G G S P I T G Y W L E K R       | ... | E E G S         | - P Y     | - W S R S R A P I T K V L G | - K G V E F N V P R L L E G           | ...                             | V K Y G F R A M A I N A G       | - I E P P S P S D P E V A K   |                                 |
| A20.3  | V P G P A P | D K P T       | ... | V S S V T R N S M T W N E E P   | I Y D G G S P V T G Y W L E M K         | ... | D T T S         | - K R     | - W K R V N R D P           | - I K A M T L G V S Y K V T G L I E G | ...                             | S D Y Q F V Y A I N A A G       | - V E P A S L P S D P A T A R |                                 |
| A27.3  | V P G P P   | G P V K       | ... | V T N I T E K M T L W D A P     | L D N G G A P I S H Y I V E R K         | ... | E T S R         | - L A     | - W A E D                   | - E D                                 | ...                             | K C E A Q S Y T A I K L I G     | - N E Y F F R V A A N E Y G   | - V G R L D S - D P V A K       |
| A34.3  | S P S P P P | G K P V       | ... | V T D I T E N A A T S W M P P   | P K S D G G S I T G Y Y M E R N         | ... | V L T G         | - T T     | - W K R V                   | - N K                                 | ...                             | T P I A D L K F R V T G L E G   | - T E Y F F R V A E N E Y G   | - I S K P S S D P I K A C       |
| A41.3  | D K P G P P | D P P E       | ... | V T K V S E E M T V W M P P     | P E Y D G G S I T G Y V L E K K         | ... | E K H S         | - T R     | - W V P V                   | - N K                                 | ...                             | S A I P E R M K V Q N L P D     | - H E Y F F R V K A E N I G   | - I E P P S L S P R V V A K     |
| A48.3  | G P S P P   | K N A R       | ... | V T K V N K D C I F A W D R     | P D S D G G S P I T G Y L I E R K       | ... | E R N S         | - L L     | - W K K A                   | - N D                                 | ...                             | T V R S T E P Y C A G L V E G   | - I E S Y F R I A E N E Y G   | - S P P S K T E P V A K         |
| A59.3  | D V P G P P | G T P E       | ... | I T M V R D S S V L T W P P     | P L D D G S P I T G Y L I E R K         | ... | E T S R         | - L       | - W T V E                   | - S E                                 | ...                             | D I O S C R H V A T K I Q G     | - N E Y F F R V A E N E Y G   | - K E G P Q S - E P V A K       |
| A70.3  | K V P G P P | G T P P       | ... | V T A V T K D S M T I S W N E P | L S D D G G S P I L G Y V E R K         | ... | E R N G         |           |                             |                                       |                                 |                                 |                               |                                 |

**Fig S2: RMSD-based calculation of the global consensus in sequence conservation in A-band FnIII domains**

**A.** RMSD values from the comparison of two PaSiMap vector maps. Blue line; RMSD values calculated between the PaSiMap output for the original, unedited MSA (native MSA) and the PaSiMap output for each derivative MSAs, where positions had been cumulatively removed in order of decreasing conservation. Red line: RMSD values calculated between the PaSiMap output for the original, unedited MSA (native MSA) and a decoy derivative MSA, where positions had been cumulatively removed at random. Here, the RMSD value shown is an average of three decoy derivative MSA generated at random; **B.** For each cumulative sequence removal, the difference between both RMSD values shown in A. (blue, red lines) is displayed. A horizontal or decreasing slope in the weighted  $\Delta$ RMSD (see Methods) curve is the point where removing a position by conservation is no longer different to removing a residue at random. This point is marked with a vertical line and corresponds to a SoP score of 0.5.



# Fig S3: Group MSA alignments of FnIII domains from titin's A-band showing consensus residues.

Positions in grey correspond to SoP scores >0.5 and were taken to constitute the global conservation consensus for A-band FnIII domains. FnIII-type specific residues are considered as those that match the criteria of a SoP > 1 and over 90% occupancy and are shown in yellow.

| Group A |                                                                                                                                                                                                                       |
|---------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| A2.1    | GLPGPC-KDIK---ASDITKSSCKLT <sup>Y</sup> EPPEFDGGTPIILHYVLERR-----EAGR--RT--YIPV--MS---GENKLSWTVKDLIPN--GEYFRVRAV <sup>Y</sup> KVG-GGEVIEL <sup>Y</sup> LKNEVIAQ <sup>Y</sup>                                          |
| A9.1    | DVPGPV-LDLK---PVVTNRKMCLLN <sup>Y</sup> SDPEDDGGSEITGFIIERK-----DAKM--HT--WRQP-----IETRSKCDITGLLEG--QYKFRVIAK <sup>Y</sup> KFG-CGPPV <sup>Y</sup> ELI-GRILAV <sup>Y</sup>                                             |
| A16.1   | DVPGPP-KDLK---VSDITRGSCLRL <sup>Y</sup> KMPDDGGDRIKGYVIEKR-----TIDG--KA--WTKV--NP---DCGSTTFFVVDLLESE--QQYFRVRAE <sup>Y</sup> NFG-IGPPV <sup>Y</sup> ETIQRTAR <sup>Y</sup>                                             |
| A23.1   | DVPGVGTFFL---ANLITNESCKLT <sup>Y</sup> FSPEDDGGSPITNYVIEKR-----ESDR--KA--WTPV--TY---TVTRQNA <sup>Y</sup> TQGLIQG--KAYFRIAAE <sup>Y</sup> NSIG-MGPPV <sup>Y</sup> ETSEALVIR <sup>Y</sup>                               |
| A30.1   | DKPGPP-RDLK---VSEIRKSDCYLT <sup>Y</sup> KEPLDGGSPITNYVVEKR-----DVAS--AQ--WSPL--SA---TSKKKSHFAKHLNEG--NQYFRVAAE <sup>Y</sup> NQYG-RGPPV <sup>Y</sup> ETPKPKAL <sup>Y</sup>                                             |
| A37.1   | DRPGPC-QNLK---VNTVKENCITIS <sup>Y</sup> ENPLDGGSEITNFIVEYR-----KPNQ--KG--WSIV--AS---DVTKRLIKA-NLLAN--NEYFRVCAE <sup>Y</sup> NKVG-VGPPV <sup>Y</sup> ETTKPILAI <sup>Y</sup>                                            |
| A44.1   | DTPGPV-SDLK---VSDVTKTSCHV <sup>Y</sup> SHAPPENDGGSQVTHYVIEKR-----EADR--KT--WSTV--TP---EVKKTSPHVTNLVPG--NEYFRVTA <sup>Y</sup> V <sup>Y</sup> EYG-PSV <sup>Y</sup> TDV <sup>Y</sup> PKPVLAS <sup>Y</sup>                |
| A55.1   | DTPGPP-INVT---VKEISKDSAYT <sup>Y</sup> HEPPIIDGGSPITNYVVEKR-----DAER--KS--WSTV--TT---ECSTKSPRVPNLEEG--KSYFRVTA <sup>Y</sup> E <sup>Y</sup> EYG-IGD <sup>Y</sup> GET <sup>Y</sup> RDADKAS <sup>Y</sup>                 |
| A66.1   | DTPGPV-LNLR---PFDITKDSVTLN <sup>Y</sup> DLPLIDGGSRITNYVIEKR-----NATR--KS--YSTA--TT---KCHKCTYKVTGLSEGG--CEYFRVMAE <sup>Y</sup> EYG-IGET <sup>Y</sup> ET <sup>Y</sup> TTEPVKAS <sup>Y</sup>                             |
| A77.1   | DTPGPP-QDLK---VKEVTKTSVTLN <sup>Y</sup> DPPLDGGSEIKNYVIEKR-----ESTR--KA--YSTV--AT---NCHKTSKVKDQIQEG--CSYFRVIAE <sup>Y</sup> EYG-IGL <sup>Y</sup> PAE <sup>Y</sup> TAEVKA <sup>Y</sup> S                               |
| A88.1   | DTPGPP-VNLR---VTEITKDSVTLN <sup>Y</sup> HEPPIIDGGSEIKNYVIEKR-----EATR--KS--YAAV--VT---NCHKNSKKIDQIQEG--CSYFRVTA <sup>Y</sup> E <sup>Y</sup> EYG-IGL <sup>Y</sup> PAE <sup>Y</sup> TADPVKA <sup>Y</sup>                |
| A99.1   | DTPGPP-QNLA---VKEVRKDSAPL <sup>Y</sup> VHEPPIIDGGAKVKNYVIDKR-----ESTR--KA--YANV--SS---KCSKTSFKVENLIEG--AIYFRVMAE <sup>Y</sup> EYG-VGV <sup>Y</sup> ETV <sup>Y</sup> TDVADKAA <sup>Y</sup>                             |
| A110.1  | DS <sup>Y</sup> PSAP-VNLT---VREVKKDSVTLN <sup>Y</sup> HEPPIIDGGAKITNYVIEKR-----ETTR--KA--YATI--TN---NCTKTTFRLENLIEG--CSYFRVLA <sup>Y</sup> E <sup>Y</sup> EYG-IGL <sup>Y</sup> PAE <sup>Y</sup> TTEPVKVS <sup>Y</sup> |
| A121.1  | DTPGPP-TNLT---VQDVTKDSVTLN <sup>Y</sup> HEPPIIDGGSPITNYVIEKR-----EASK--KA--YANV--SS---NCHKTSKVKDQIQEG--AIYFRVMAE <sup>Y</sup> EYG-VGV <sup>Y</sup> ETV <sup>Y</sup> TDVADKAA <sup>Y</sup>                             |
| A132.1  | DT <sup>Y</sup> PAAC-QKIQ---VKHVSRTSVTLN <sup>Y</sup> HEPPIIDGGSPITNYVIEKR-----DATK--RT--WQV--SH---KCSSTSPKIDLSEK--TFFFRVLA <sup>Y</sup> E <sup>Y</sup> EYG-IGET <sup>Y</sup> ET <sup>Y</sup> TTEPVKAA <sup>Y</sup>   |
| A143.1  | DTPGPP-GPIT---FKDVTGRSATL <sup>Y</sup> NHAPLIDGGARINHYVVEKR-----EASR--RS--WQVI--SE---KCTRQIFKVNDLAEG--VPYFRVSA <sup>Y</sup> V <sup>Y</sup> EYG-VGE <sup>Y</sup> ET <sup>Y</sup> YMPPEVIA <sup>Y</sup> T               |
| A154.1  | DTPGPC-PSVK---VKEVSRDSVTI <sup>Y</sup> NHEPPIIDGGAPINNYVIEKR-----EAM--RA--FKTV--TT---KCSKTLYRISGLVEG--TMHYFRVLP <sup>Y</sup> E <sup>Y</sup> EYG-IGET <sup>Y</sup> ET <sup>Y</sup> SDAVLVS <sup>Y</sup>                |
| A5.3    | DTPGPP-INPV---FEDIRKTSVLCK <sup>Y</sup> HEPPIIDGGSEIINHYTLEKK-----DKTKDSE--WIVV--TS---TLRHCKYSVTKLIEGGPKYELFRVRAE <sup>Y</sup> RFG-PGPP <sup>Y</sup> CVS--KPLVAK <sup>Y</sup>                                         |
| A12.3   | DRPGPP-RNLA---VTDIKAESCYLT <sup>Y</sup> NHAPLIDGGSEIINHYVIDKR-----DASR--KKAEEV--TN---TAVKERYGLWKLIPN--GQYFRVRAV <sup>Y</sup> NKYG-IGSD <sup>Y</sup> CHS--DKVVIQ <sup>Y</sup>                                          |
| A19.3   | GRPGPPVGPPIK---FESVSAQDMTL <sup>Y</sup> FPPKDDGGSEIINHYVIEKR-----EANN--KT--WVHV--SS---EPKECTYTIPKILEG--HEYFRVMAQ <sup>Y</sup> NKYG-VG <sup>Y</sup> ETV <sup>Y</sup> TDVADKAA <sup>Y</sup>                             |
| A26.3   | DHPGPPVGPVVS---FDEVTKDYMVIS <sup>Y</sup> KPPLDGGSEIINHYTLEKK-----EYKG--DV--WMPV--TS---ASAKTCKVKSLIEG--KDYFRVIAE <sup>Y</sup> NKYG-IGSD <sup>Y</sup> CHS--DSMKAR <sup>Y</sup>                                          |
| A33.3   | DVPGPPGTGPIK---LDVTPFHMHTIS <sup>Y</sup> QPPKDDGGSPVINYVEKQ---DTRK--RT--WQV--SS---GSKTKLKIPLIQG--CEYFRVRAE <sup>Y</sup> NKYG-VGPP <sup>Y</sup> VS--TPVAK <sup>Y</sup>                                                 |
| A40.3   | DKPGPV-RNLK---IVDVSDDRCV <sup>Y</sup> CHDPEDDGGGEIQNYILEK---EKKR--MV--WSTY--SA---TVLTPGT <sup>Y</sup> TVTRLIEG--NEYFRVRAE <sup>Y</sup> NKYG-TGPP <sup>Y</sup> TS--KPIVIAK <sup>Y</sup>                                |
| A47.3   | DA <sup>Y</sup> PGPPQPFDF---ISDDADGSPV <sup>Y</sup> SHPLEDGGSEIINHYVEK---DVSRR--GD--WVTA--LA---SVTKTS <sup>Y</sup> CRVGLIIEG--QYIFRVAE <sup>Y</sup> RFG-ISE <sup>Y</sup> ELS--PKHVAQ <sup>Y</sup>                     |
| A58.3   | GK <sup>Y</sup> IGIPTGPIK---FDEVTAEMTL <sup>Y</sup> KAPPKDDGGSEIINHYTLEKK-----DQVN--NK--WVTC--AS---AVQKTTF <sup>Y</sup> RVTRLIEG--MEYFRVSAE <sup>Y</sup> NKYG-VGE <sup>Y</sup> ELS--EPVIAK <sup>Y</sup>               |
| A69.3   | IDPGPPGTGPIK---FESVSDSFVTF <sup>Y</sup> SHDPENDGGGFISHYVVEKR-----QDSS--TT--WVEL--AT---TVIRTTYKATRLTGG--LEYFRVAKQ <sup>Y</sup> NKYG-VG <sup>Y</sup> ETV <sup>Y</sup> TDVADKAA <sup>Y</sup>                             |
| A80.3   | DKPGPPGTGPIK---FDEVTAEMTL <sup>Y</sup> KAPPKDDGGSEIINHYTLEKK-----DQVN--NK--WVTC--AS---AVQKTTF <sup>Y</sup> RVTRLIEG--MEYFRVSAE <sup>Y</sup> NKYG-VGE <sup>Y</sup> ELS--EPVIAK <sup>Y</sup>                            |
| A91.3   | DKPGPPKGPVK---FDEVSAESITLS <sup>Y</sup> NPPLYTGGCQITNYVIEKR-----DITT--TV--WDVV--SA---TVARTTKVTKIKTGG--TEYFRVIAE <sup>Y</sup> NKYG-KSA <sup>Y</sup> ELS--DPIVAQ <sup>Y</sup>                                           |
| A102.3  | EKPGPPVGPVIR---FDEVSAESITLS <sup>Y</sup> NPPLYTGGCQITNYVIEKR-----DITT--TV--WDVV--SA---TVARTTKVTKIKTGG--TEYFRVIAE <sup>Y</sup> NKYG-KSA <sup>Y</sup> ELS--DPIVAQ <sup>Y</sup>                                          |
| A113.3  | DKPGPP-GPIR---FDEVSCDSITIS <sup>Y</sup> NPPEDGGCQISNYVEK---EETS--TT--WHIV--SQ---AVARTSKIVRLTGG--SEYFRVCAE <sup>Y</sup> NKYG-KSS <sup>Y</sup> ELS--SAVVAE <sup>Y</sup>                                                 |
| A124.3  | DRPGPPGTGPIK---FDEVSAESITLS <sup>Y</sup> NPPLYTGGCQITNYVIEKR-----DITT--TV--WDVV--SA---TVARTTKVTKIKTGG--TEYFRVIAE <sup>Y</sup> NKYG-KSA <sup>Y</sup> ELS--DPIVAQ <sup>Y</sup>                                          |
| A135.3  | GRPGPPGTGPIK---FDEVSAESITLS <sup>Y</sup> NPPLYTGGCQITNYVIEKR-----DITT--TV--WDVV--SA---TVARTTKVTKIKTGG--TEYFRVIAE <sup>Y</sup> NKYG-KSA <sup>Y</sup> ELS--DPIVAQ <sup>Y</sup>                                          |
| A146.3  | GRPGPPGTGPIK---FDEVSAESITLS <sup>Y</sup> NPPLYTGGCQITNYVIEKR-----DITT--TV--WDVV--SA---TVARTTKVTKIKTGG--TEYFRVIAE <sup>Y</sup> NKYG-KSA <sup>Y</sup> ELS--DPIVAQ <sup>Y</sup>                                          |
| A157.3  | DKPGPPGTGPIK---FDEVSAESITLS <sup>Y</sup> NPPLYTGGCQITNYVIEKR-----DITT--TV--WDVV--SA---TVARTTKVTKIKTGG--TEYFRVIAE <sup>Y</sup> NKYG-KSA <sup>Y</sup> ELS--DPIVAQ <sup>Y</sup>                                          |
| A51.3   | DKPGPP-ASVK---INKNYSRDLRL <sup>Y</sup> HEPPIIDGGSEIINHYVIDKR-----EESR--PN--WQV--SA---TVPTTS <sup>Y</sup> CSVEKILEG--HEYFRVIAE <sup>Y</sup> NKYG-VGD <sup>Y</sup> ELS--EPVIAK <sup>Y</sup>                             |
| A62.3   | DVPGPP-GPIV---INKNYSRDLRL <sup>Y</sup> HEPPIIDGGSEIINHYVIDKR-----EESR--PN--WQV--SA---TVPTTS <sup>Y</sup> CSVEKILEG--HEYFRVIAE <sup>Y</sup> NKYG-VGD <sup>Y</sup> ELS--EPVIAK <sup>Y</sup>                             |
| A73.3   | DRPGPPGTGPIK---FDEVSAESITLS <sup>Y</sup> NPPLYTGGCQITNYVIEKR-----DITT--TV--WDVV--SA---TVARTTKVTKIKTGG--TEYFRVIAE <sup>Y</sup> NKYG-KSA <sup>Y</sup> ELS--DPIVAQ <sup>Y</sup>                                          |
| A84.3   | DRPGPPGTGPIK---FDEVSAESITLS <sup>Y</sup> NPPLYTGGCQITNYVIEKR-----DITT--TV--WDVV--SA---TVARTTKVTKIKTGG--TEYFRVIAE <sup>Y</sup> NKYG-KSA <sup>Y</sup> ELS--DPIVAQ <sup>Y</sup>                                          |
| A95.3   | DRPGPPGTGPIK---FDEVSAESITLS <sup>Y</sup> NPPLYTGGCQITNYVIEKR-----DITT--TV--WDVV--SA---TVARTTKVTKIKTGG--TEYFRVIAE <sup>Y</sup> NKYG-KSA <sup>Y</sup> ELS--DPIVAQ <sup>Y</sup>                                          |
| A106.3  | DRPGPPGTGPIK---FDEVSAESITLS <sup>Y</sup> NPPLYTGGCQITNYVIEKR-----DITT--TV--WDVV--SA---TVARTTKVTKIKTGG--TEYFRVIAE <sup>Y</sup> NKYG-KSA <sup>Y</sup> ELS--DPIVAQ <sup>Y</sup>                                          |
| A117.3  | DKPGPPGTGPIK---FDEVSAESITLS <sup>Y</sup> NPPLYTGGCQITNYVIEKR-----DITT--TV--WDVV--SA---TVARTTKVTKIKTGG--TEYFRVIAE <sup>Y</sup> NKYG-KSA <sup>Y</sup> ELS--DPIVAQ <sup>Y</sup>                                          |
| A128.3  | DKPGPPGTGPIK---FDEVSAESITLS <sup>Y</sup> NPPLYTGGCQITNYVIEKR-----DITT--TV--WDVV--SA---TVARTTKVTKIKTGG--TEYFRVIAE <sup>Y</sup> NKYG-KSA <sup>Y</sup> ELS--DPIVAQ <sup>Y</sup>                                          |
| A139.3  | DTPGKVVGTGPIK---FDEVSAESITLS <sup>Y</sup> NPPLYTGGCQITNYVIEKR-----DITT--TV--WDVV--SA---TVARTTKVTKIKTGG--TEYFRVIAE <sup>Y</sup> NKYG-KSA <sup>Y</sup> ELS--DPIVAQ <sup>Y</sup>                                         |
| A150.3  | DS <sup>Y</sup> PGPP-GKLT---VSRVTQEKCTL <sup>Y</sup> SLPQEDGGCAEITHYVIEKR-----EESR--PN--WQV--SA---TVPTTS <sup>Y</sup> CSVEKILEG--HEYFRVIAE <sup>Y</sup> NKYG-VGD <sup>Y</sup> ELS--EPVIAK <sup>Y</sup>                |
| A161.3  | GS <sup>Y</sup> PNSEPGPIK---YDDTQVRSVRV <sup>Y</sup> SRPPADGGADILGYILEKRR-----EYK--AA--WYTI--DS---RVGRTSLVVKGLKEN--VEYHFRVSAE <sup>Y</sup> NQFG-ISK <sup>Y</sup> ELS--SEEPV <sup>Y</sup> TPK <sup>Y</sup>             |
| Group B |                                                                                                                                                                                                                       |
| A6.4    | FFPDAP-DKPI---VEDTNSMVLK <sup>Y</sup> WNEPK-DNGSPILGYWLEKRR-----EVNS--TH--WSRV--NK---SLNALKANVDGLLEG--LTYFRVCAE <sup>Y</sup> NAA-GPK <sup>Y</sup> TS--PSDPKTAH <sup>Y</sup>                                           |
| A13.4   | RLPGPP-GKPK---VLARTKGSMLV <sup>Y</sup> SNTPPLDGGSPITGYWLEKRR-----EGGS--PY--WSRVRAPI <sup>Y</sup> TKVGLKGVETNVPRLIEG--VKYFRAMAE <sup>Y</sup> NAA-IGPP <sup>Y</sup> SPSDPFAVAG <sup>Y</sup>                             |
| A20.4   | SVPGAP-DKPT---VSSVTRNSMTV <sup>Y</sup> NHEPEYDGGSPVITGYWLEKRR-----DTTS--KR--WKRVRNP <sup>Y</sup> IKAMTLGVSVKVTGLIEG--SDYFRVYAE <sup>Y</sup> NAA-VGPAS <sup>Y</sup> PSDPFATAR <sup>Y</sup>                             |
| A27.4   | RVPDAP-DQPI---VTEVTKDSALVT <sup>Y</sup> NKHPDGGKPIITHYILEKRR-----TMS--KR--WAKVTDP <sup>Y</sup> ---INPYTKFRVPDLIEG--CQYFRVSAE <sup>Y</sup> IEG-IGD <sup>Y</sup> PS <sup>Y</sup> PSKPVFAK <sup>Y</sup>                  |
| A34.4   | SPSPPP-GKPV---VTDITENAAVT <sup>Y</sup> SNLTPKSDGGSPITGYWLEKRR-----EYTG--K--WVRV--NK---TPADLKFRVTGLIEG--NTYFRVFAE <sup>Y</sup> NLA-LSK <sup>Y</sup> PS <sup>Y</sup> SDPFIKAC <sup>Y</sup>                              |
| A41.4   | DKPGRP-DPPE---VTKVSKKEMTV <sup>Y</sup> VNPPEDDGGSEITGYFLEKRR-----EKHS--TR--WVVP--NK---SAIPERRKHKVQNLDP--HEYFRVKA <sup>Y</sup> IEG-IGET <sup>Y</sup> SPSRPVVAK <sup>Y</sup>                                            |
| A48.4   | GV <sup>Y</sup> SEP-KNAR---VTKVKNKDCIFV <sup>Y</sup> ANDRPDSDGGSPITGYLIERK-----ERNSS--LL--WVKA--ND---TLVRS <sup>Y</sup> TEYPCAGLVEG--LEYFRVIAE <sup>Y</sup> NAA-GSP <sup>Y</sup> SPTEYVTA <sup>Y</sup> R              |
| A59.4   | DV <sup>Y</sup> PDAP-PPP---VGVRAHDSVSL <sup>Y</sup> TMDPKKTGGSPITGYHLEKRR-----ERNSS--LL--WVKA--NK---TPIRMRD <sup>Y</sup> FKVTGLIEG--LEYFRVMAE <sup>Y</sup> NLA-VGK <sup>Y</sup> PS <sup>Y</sup> SEPVAL <sup>Y</sup>   |
| A70.4   | KVPGPP-GTPQ---VAVTKDSMTI <sup>Y</sup> SNHEPLSDGGSPILGYHLEKRR-----ERNSS--LL--WVKA--NK---TPIRMRD <sup>Y</sup> FKVTGLIEG--LEYFRVMAE <sup>Y</sup> NLA-VGK <sup>Y</sup> PS <sup>Y</sup> SEPVAL <sup>Y</sup>                |
| A81.4   | KVPGPP-GTPV---VTLSSRDSMEVQ <sup>Y</sup> NHEPISDGGSRVIGYHLEKRR-----ERNSS--LL--WVKA--NK---TPIPQTK <sup>Y</sup> FKTTGLIEG--VEYFRVSAE <sup>Y</sup> IVG-IGK <sup>Y</sup> PS <sup>Y</sup> SECVVAV <sup>Y</sup>              |
| A92.4   | KEPGPP-GTPF---VATISKDSMVQ <sup>Y</sup> NHEPVNNGGSPVIGYHLEKRR-----ERNSS--LL--WVKA--NK---TIIHDT <sup>Y</sup> QFKAQNLIEG--IEYFRVYAE <sup>Y</sup> IVG-VGK <sup>Y</sup> PS <sup>Y</sup> SECVVAV <sup>Y</sup>               |
| A103.4  | KEPGPP-GTPF---VATISKDSMVQ <sup>Y</sup> NHEPVNNGGSPVIGYHLEKRR-----ERNSS--LL--WVKA--NK---TIIHDT <sup>Y</sup> QFKAQNLIEG--IEYFRVYAE <sup>Y</sup> IVG-VGK <sup>Y</sup> PS <sup>Y</sup> SECVVAV <sup>Y</sup>               |
| A114.4  | SPPGPP-GTPK---VVAHATKSTMLV <sup>Y</sup> TNQPVNDDGGSRVIGYHLEKRR-----ERNSS--LL--WVKA--NK---ILADT <sup>Y</sup> QVKSGLIEG--LMYFRVYAE <sup>Y</sup> IVG-IGK <sup>Y</sup> PS <sup>Y</sup> SECVVAV <sup>Y</sup>               |
| A125.4  | TPPGPP-STPW---VNTVRESITV <sup>Y</sup> GNHEPVNNGGSAVVGYHLEKRR-----ERNSS--LL--WVKA--NK---LVIRTH <sup>Y</sup> FKVTTISAG--LEYFRVYAE <sup>Y</sup> IVG-VGK <sup>Y</sup> PS <sup>Y</sup> SECVVAV <sup>Y</sup>                |
| A136.4  | RIPGPP-GKPV---VYNTSDGMSLT <sup>Y</sup> MDAPVYDGGSEVTGFHVEKRR-----ERNSS--LL--WVKA--NK---SPISGR <sup>Y</sup> YRATGLIEG--LDYFRVYAE <sup>Y</sup> IVG-VGK <sup>Y</sup> PS <sup>Y</sup> SECVVAV <sup>Y</sup>                |
| A147.4  | VPSAP-TRPE---VYHSANAMS <sup>Y</sup> IRHEPEYDGGSEITGYWLEKRR-----ERNSS--LL--WVKA--NK---SPISGR <sup>Y</sup> YRATGLIEG--LDYFRVYAE <sup>Y</sup> IVG-VGK <sup>Y</sup> PS <sup>Y</sup> SECVVAV <sup>Y</sup>                  |
| A158.4  | RIPGPP-ETLQ---FDSRSDGMTL <sup>Y</sup> WYPPEDDGGSPVITGYVIEKR-----EYRA--DR--WVRV--NK---VPVMT <sup>Y</sup> TRSTGLIEG--LEYFRVTA <sup>Y</sup> IVG-VGK <sup>Y</sup> PS <sup>Y</sup> SECVVAV <sup>Y</sup>                    |
| A52.4   | DPGRC-DPPV---ISNITKDMHTV <sup>Y</sup> SNKPPADGGSPITGYLIERK-----ETQA--VN--WTKV--NR---KPIERT <sup>Y</sup> LKATGLIEG--TEYFRVTA <sup>Y</sup> IVG-VGK <sup>Y</sup> PS <sup>Y</sup> SECVVAV <sup>Y</sup>                    |
| A63.4   | GP <sup>Y</sup> PGPP-EKPE---VSNVTKNTATV <sup>Y</sup> SNKRPVDDGGSEITGYHVEKRR-----EKKS--LR--WVRA--IK---TPVSD <sup>Y</sup> LRKVTGLIEG--STYFRVSAE <sup>Y</sup> NAA-IGPP <sup>Y</sup> SPSDPFAVAG <sup>Y</sup>              |
| A74.4   | GP <sup>Y</sup> DPDP-KNPE---VTTITKDSMVV <sup>Y</sup> CHGHPDSDGGSEIINHYVIEKR-----DKAG--QR--WIKC--NK---KTLTDL <sup>Y</sup> RYKVSGLIEG--HEYFRVMAE <sup>Y</sup> NAA-IGAP <sup>Y</sup> SPSPFYKAC <sup>Y</sup>              |
| A85.4   | VVPDAP-KAPE---VTTVTKDSMVV <sup>Y</sup> CHGHPDSDGGSEIILGYVLEKRR-----DEKG--IR--WTRC--NK---RLIGEL <sup>Y</sup> RLRVTLIEG--HDYFRVSAE <sup>Y</sup> NAA-LSEP <sup>Y</sup> SPSAYKAC <sup>Y</sup>                             |
| A96.4   | VLP <sup>Y</sup> PGPP-KSLE---FTVITAKDSMTV <sup>Y</sup> CHGHPDSDGGSEIILGYVLEKRR-----DEKG--IR--WTRC--NK---RLIGEL <sup>Y</sup> RLRVTLIEG--HDYFRVSAE <sup>Y</sup> NAA-LSEP <sup>Y</sup> SPSAYKAC <sup>Y</sup>             |
| A107.4  | KPPGPP-STPE---VSAITKDSMVV <sup>Y</sup> CHGHPDSDGGSEIILGYVLEKRR-----DEKG--IR--WTRC--NK---KTLTDL <sup>Y</sup> RLRVTLIEG--HEYFRVMAE <sup>Y</sup> NAA-VGEP <sup>Y</sup> SPSPFYKAC <sup>Y</sup>                            |
| A118.4  | TPSPPP-TSLE---VTSVTKESMTL <sup>Y</sup> CHSRPESDGGSEISGYIIEKRR-----EKNS--LR--WVRV--NK---KPVYDL <sup>Y</sup> RVKSTGLIEG--CEYFRVYAE <sup>Y</sup> IVG-LSL <sup>Y</sup> PS <sup>Y</sup> ETSPVIRAB <sup>Y</sup>             |
| A129.4  | VT <sup>Y</sup> PGPP-GIPE---VNTITKNSMTV <sup>Y</sup> SNRPIADGGSDISGYFLEKRR-----DKKS--LG--WFKV--IK---ETIRDT <sup>Y</sup> QKVTGLIEG--SDYFRVCAV <sup>Y</sup> NAA-QGPP <sup>Y</sup> SPSEFVKA <sup>Y</sup>                 |
| A140.4  | VTPDAP-GIPE---VNTITKNSMTV <sup>Y</sup> SNRPIADGGSDISGYFLEKRR-----DKKS--LG--WFKV--IK---ETIRDT <sup>Y</sup> QKVTGLIEG--SDYFRVCAV <sup>Y</sup> NAA-QGPP <sup>Y</sup> SPSEFVKA <sup>Y</sup>                               |
| A151.4  | TPSPPP-GIPE---VNTITKNSMTV <sup>Y</sup> SNRPIADGGSDISGYFLEKRR-----DKKS--LG--WFKV--IK---ETIRDT <sup>Y</sup> QKVTGLIEG--SDYFRVCAV <sup>Y</sup> NAA-QGPP <sup>Y</sup> SPSEFVKA <sup>Y</sup>                               |
| A162.4  | NPEPPSPNPE---VLDVTKESMTL <sup>Y</sup> CHSRPESDGGSEISGYIIEKRR-----DKKS--LG--WFKV--IK---ETIRDT <sup>Y</sup> QKVTGLIEG--SDYFRVCAV <sup>Y</sup> NAA-QGPP <sup>Y</sup> SPSEFVKA <sup>Y</sup>                               |

## Group C

A12\_2 QPDDPP-VDVE---VHNPTAEAMTITWKPLLDGGGSKIMGYIIEKI-----AKGE--ER---WKR--NE---HLVPILTYTAKGLEEG--KEYQFRVRAENAAQ--ISEPSATPTPKAY-  
 A10\_2 DPLGPP-TSPERLITYTERQRTTITLWKKPRNGGSGPIQGYIIEKR-----RDK--PD--FRV--NK---RLCPTTSPLVENIDEH--QMYEPRVAVNEIG--ESEPSPLNVVIOD-  
 A17\_2 YPDDPP-IKLE---IGLITKNTVHLNKKPKNDGGSVTHYIVLECLAWDPTGKK--EA---WQRC--NK---RDVEELQPTVEDIVLEGG--GEYEFPRVAVNAAG--VSKPSATVGPDDCO-  
 A24\_2 TVDERP-EDLE---KDVTKNTVTLWNPKYDGGSEIINYVLESR-----LGT--EK--FKHV--TN---DNLLSRKYTVKGLKEG--DTYEFVRSVAVNIGV--QKPSCTKPRITCK-  
 A31\_2 HPPGPP-KDLH---HVDVDTKEVSLVWNPDRDGGSPITGYLVEYQ-----EGT--QD--WKKF--KT---VTNLECVVTVGLQGG--KTYEPRVKAENIGV--LGLP--DTTPEICO-  
 A38\_2 DRPGEP-ENLH---IADKGKFFVYLKRRPDYDGGSENLSYHVERR-----LGS--DD--WERV--HK---GSIKETHYMVDRVCVEN--QYEFVQTKNEGG--ESDVRVTEEVVKE-  
 A45\_2 SEPDDPP-RKLE---ATEMTKNSATLANLPLLDGGGAKIDGYIISYR-----EEQPADR--WTEY--SV---VKDLSLVVTVGLKEG--KKYKFRVAARNAVG--VSLFRVAEGVVYAK-  
 A56\_2 QTPGPP-VDLK---VRSVSKSSCSIGNKKPHSDGGSRIGYVVDL-----TENK-----WQRV--MK---SLSLQYSAKDLTEG--KEYTFRVSAENENG--EGPSEI--TVVAR-  
 A67\_2 EAPSP-DSLH---IMDITKSTVSLANPKPKHDGGSKITGYVIEAQ-----RGS--DQ--WTHI--TT---VKGLECVVRNLTGEG--EETITQVMAVNASAG--RSAPRES--RPVIVK-  
 A78\_2 ERLP-CKIT---IMDVTRNSVSLNKKPEHDGGSKITGYIVEMQ-----TKGS--DK--WATC--AT---VKVTEATITGLIQG--EYSFRVSAQNEGS--LSDRGLSVFVIK-  
 A89\_2 EVFGPP-CKIT---IMDVTRNSVSLNKKPEHDGGSKITGYIVEMQ-----AKHS--EK--WSEC--AR---VKSLQAVITNLITG--EYLFPRVAVNEKG--RSDRGLSVFVIK-  
 A100\_2 EPPSP-CKVT---LTDVSQTSASLWNEKPEHDGGSRVGLGYVEMQ-----PKGT--EK--WSLV--AE---SKVCNAVVTGISSG--QYQFRVAVNEKG--RSDRGLSVFVIK-  
 A111\_2 EPLP-GRVT---LVDVTRNTATIKWKEPEHDGGSKITGYVEMQ-----TKGS--EK--WSTC--TQ---VKVTEATITGLITAG--EYVFRVAVNEKG--RSDRGLSVFVIK-  
 A122\_2 EKSP-CKLG---VTSISKDSVSLTWLKEPEHDGGSRIVHYVVEAL-----EKQ--KN--WVKC--AV---AKSTHVVSGLRNEN--SEYFPRVAVNEAG--LSDRGLSVFVIK-  
 A133\_2 EPPAPI-RDLS---MKDSTKTSVLSLWTKPDHDGGSVITEYVVERK-----GKE--QT--WSHA-----GISKTCEIEVSQLEKQ--SVLEFRVFAKNEKG--LSDRGLSVFVIK-  
 A144\_2 EQPAPP-RLLD---VVDTSKSSAVLANLKKPDHDGGSRITGYLLEMR-----QGS--DL--WVEA--GH---TKQLTFTVERLVEK--TEYEFPRVAKNDAG--YSEPRFAFSSVILK-  
 A155\_2 EPLVP-AKLE---VVDVTKSTVTLWNEKPLDGGSRITGYVLEAC-----KAGT--ER--WMKV--VT---LKPVTLEHTVTSINLEG--EQYLFRIQAQNEKG--YSEPRFAFSSVILK-  
 7\_5 SPFGPP--IPR---VTDTSSTTIELEWEPFAHGGGEIVGYFVDKQ-----LVGT--NK--WSRC--TE---KMKVQRQTVKKEIREG--ADYKLRVSAVNAAG--EGPFGGT--QPVTVK-  
 A14\_5 FPGPP-SCPE---VMDKTKSSISLGNKPPAKDGGSPFKGYVEMQ-----EGT--TD--WKR--NE--PDKLITCECVVPLNKL--RKTFRVAVNEAG--ESEPSDTTGEIPAT-  
 A21\_5 APFGPP--FKK---VTDWTKSSADLWSPPLDGGSEVTVGYIYEK-----EGK--EE--WKKG--KD---KEVRGTLVVTGLKEG--AFYKFRVSAVNAAG--LGEQGVTDVEMK-  
 A28\_5 AKSP-VPNE---AIDTTCSVDLWQPPRHDDGGSKILGYIYEQ-----KVG--EE--WRR--NH--TPESCPEPTKYKVTGLRDG--QTYKFRVAVNAAG--ESDRAVPEPVLK-  
 A35\_5 KPFGPP--INPK---LKDKSRETADLVNTKPLDGGSPILGYVVECC-----KPT--AQ--WNRI--NK--DELIQCAFRVPGILIEG--NEYFRVAKNIGV--EGERELAEVIAK-  
 A42\_5 EPPGPP--TNFR---VDDTTKHSITLWNEKPLDGGSPILGYVVECC-----KPT--AQ--WNRI--NK--DELIQCAFRVPGILIEG--NEYFRVAKNIGV--EGERELAEVIAK-  
 A49\_5 MPVDP-CKPE---VIDVTKSTVSLWNEKPPAKDGGSKIGYFVEAC-----LPG--DK--WVR--NT--APHQIPQEEYTATGLEEK--AQYQFRAIARTAVN--ISPPSPSPDPVTIL-  
 A60\_5 DPLDP-CKPE---VINITRNSVTILWTEPKYDGGHKLTVGYIYEK-----LPS--KS--WMKA--NH---VNVPECAFTVTDLVEG--GKYEFRIAKNTAGAIAS--STETIICK-  
 A71\_5 DPLDP-CKPV---PLNITRHTVTILWNEKPPYDGGFKITSYIYEK-----LPN--GR--WLKA--NF---SNILENEFTVSGLTED--AAEFVRIAKNAAAGIS--SPSPDAITCR-  
 A82\_5 DPCDP-GRPE---AIVTRNSVTILWNEKPPYDGGSKITGYIYEK-----LPE--GR--WMKA--SF---THIDTHFEVTVGLVED--HRTFRIAKNAAAGVSE--STGATAR-  
 A93\_5 DPCDP-GRPE---FIMVKNRNEITLWNEKPPYDGGSKITGYIYEK-----LPE--GR--WMKA--SF---THIDTHFEVTVGLVED--HRTFRIAKNAAAGVSE--STGATAR-  
 A104\_5 DPCDP-GRPE---AIVTRNSVTILWNEKPPYDGGSKITGYIYEK-----LPE--GR--WMKA--SF---THIDTHFEVTVGLVED--HRTFRIAKNAAAGVSE--STGATAR-  
 A115\_5 DPCDP-GRPE---AIVTRNSVTILWNEKPPYDGGSKITGYIYEK-----LPE--GR--WMKA--SF---THIDTHFEVTVGLVED--HRTFRIAKNAAAGVSE--STGATAR-  
 A126\_5 DPCDP-GRPE---AIVTRNSVTILWNEKPPYDGGSKITGYIYEK-----LPE--GR--WMKA--SF---THIDTHFEVTVGLVED--HRTFRIAKNAAAGVSE--STGATAR-  
 A137\_5 SPVDP-CTPD---VIDVTRSTITLWNEKPPYDGGSKIVGYIYERK-----QGN--ER--WVR--NF---TDVSECQTVTVGLSEG--DRYEFRIAKNAAAGVSE--STGATAR-  
 A148\_5 NPVDP-GRPE---VIDVTRSTITLWNEKPPYDGGSKIVGYIYERK-----QGN--ER--WVR--NF---TDVSECQTVTVGLSEG--DRYEFRIAKNAAAGVSE--STGATAR-  
 A159\_5 APGPK-QNPR---VDDTTKHSITLWNEKPPYDGGSKIVGYIYERK-----QGN--ER--WVR--NF---TDVSECQTVTVGLSEG--DRYEFRIAKNAAAGVSE--STGATAR-  
 A53\_5 YFPAPP-AFPK---VYDTRSSVSLSNGKPAVDGGSPILGYLVEVK-----RADS--DN--WVR--NL--PQNLQKTRFEVTVGLMED--TQYQFRVAVNKGIG--YSDPSVDPKHYPK-  
 A64\_5 YFPAPP-SNPH---VYDTRSSVSLSNGKPAVDGGSPILGYLVEVK-----RADS--DN--WVR--NL--PQNLQKTRFEVTVGLMED--TQYQFRVAVNKGIG--YSDPSVDPKHYPK-  
 A75\_5 FKPGPP-GNPR---VLDTSRSSISIANKPIHDGGSEITGYVVEIA-----LPE--DE--WQIV--TP--PAGLKATSTITGLTEN--QETKIRIYAMNSES--LGEAVVPGTFKAE-  
 A86\_5 YKPGPP--NNPK---VLDTSRSSVFLSKPIHDGGCEIQGYIYEC-----QVNV--GE--WTKC--TP--PTGINKTNIEVEKLLK--HEYNFRICAINKAG--VGEIAVPGPIVE-  
 A97\_5 FKPGPP-TNAH---VYDTRSSVSLSNGKPAVDGGSPILGYLVEVK-----RADS--DN--WVR--NL--PQNLQKTRFEVTVGLMED--TQYQFRVAVNKGIG--YSDPSVDPKHYPK-  
 A108\_5 YPFGPP-SNPK---VYDTRSSVSLSNGKPAVDGGSPILGYLVEVK-----RADS--DN--WVR--NL--PQNLQKTRFEVTVGLMED--TQYQFRVAVNKGIG--YSDPSVDPKHYPK-  
 A119\_5 FLSP-CKPK---VDSGKTTITLWNEKPPYDGGAPITGYIYERK-----KDD--TD--WTKC--TQ---SLRGTETITSGITG--AEYFRVAVNKGIG--YSDPSVDPKHYPK-  
 A130\_5 DPGPP-AKR---VDSGKTTITLWNEKPPYDGGAPITGYIYERK-----KDD--TD--WTKC--TQ---SLRGTETITSGITG--AEYFRVAVNKGIG--YSDPSVDPKHYPK-  
 A141\_5 NPPGPP-TVVK---VDSGKTTITLWNEKPPYDGGAPITGYIYERK-----KDD--TD--WTKC--TQ---SLRGTETITSGITG--AEYFRVAVNKGIG--YSDPSVDPKHYPK-  
 A152\_5 YTPGPP-SAPR---VYDTRSSVSLSNGKPAVDGGSPILGYLVEVK-----RADS--DN--WVR--NL--PQNLQKTRFEVTVGLMED--TQYQFRVAVNKGIG--YSDPSVDPKHYPK-  
 A163\_5 DKPSQP-GELE---ILSISKDSVTLWNEKPEHDGGSKILGYVVEYR-----QSGD--SA--WKK--NK---ERIKDKQFTIGGLEA--TEYEFVRAENETG--LSRPRRTAMSITK-

**Fig S4: Sequence consensus for domain position within the C-zone super-repeat.**

Residues conserved globally and within the FnIII-type plus those also conserved within each subgroup are shown in grey. Residues specific to each domain position within the super-repeat (selected according to the criteria of a SoP > 1, at least 90% occupancy of the position and at least 70% sequence identity) are shown in orange.

**Type A subgroups**

|         |    |       |      |     |                |    |         |           |      |      |      |      |     |     |    |       |     |           |     |     |      |        |     |    |      |        |           |
|---------|----|-------|------|-----|----------------|----|---------|-----------|------|------|------|------|-----|-----|----|-------|-----|-----------|-----|-----|------|--------|-----|----|------|--------|-----------|
| A55_1'  | DT | PGPP  | INVT | --- | VKEISKDSAYVTE  | PP | IIDGGSP | IIINYVQKR | ---- | DAER | -KS- | WSTV | -TT | --- | EC | SKTS  | FRV | PNLEEG    | --- | KSY | FFRV | FAENEY | --- | IG | DP   | GETR   | DAVKAS    |
| A66_1'  | DT | PGPV  | LNLR | --- | PTDITKDSVTLHWD | PL | IDGGSR  | ITNYIVEKR | ---- | ETR  | -KS- | YSTA | -TT | --- | K  | CHCT  | YK  | VTGLSE    | --- | CY  | FFRV | MAENEY | --- | IG | EP   | TET    | TPVKAS    |
| A77_1'  | DT | PGPP  | QDLK | --- | VEVTKTSVTLTWD  | PL | IDGGSK  | IKNYIVEKR | ---- | ESTR | -KA- | YSTV | -AT | --- | N  | CHKS  | SW  | KDQLQEG   | --- | CY  | YFRV | LAENEY | --- | IG | LP   | AET    | AEVKAS    |
| A88_1'  | DT | SPPP  | VNLK | --- | VEITKDSVSIWTE  | PL | IDGGSK  | IKNYIVEKR | ---- | ETR  | -KS- | YAAV | -VT | --- | N  | CHKS  | SW  | KIDQLQEG  | --- | CY  | YFRV | TAENEY | --- | IG | LP   | AQ     | TADPIKVA  |
| A99_1'  | DT | PGPP  | QNLK | --- | VEVRKDSAFVLWE  | PP | IIDGGAK | VNYVIDKR  | ---- | ESTR | -KA- | YANV | -SS | --- | K  | SKTS  | FFK | VNLTG     | --- | AI  | YFRV | MAENEF | --- | VG | FP   | VE     | TDAVKA    |
| A110_1' | DS | PSAP  | VNLT | --- | REVKKDSVTLWE   | PL | IDGGAK  | ITNYIVEKR | ---- | ETTR | -KA- | YATI | -TN | --- | N  | CTKT  | FF  | FRIENLQEG | --- | CY  | YFRV | LAENEY | --- | IG | LP   | AET    | TPVKVS    |
| A121_1' | DT | PGPP  | TNIT | --- | VQDVTKEAVLSWD  | VP | ENDGGAP | VKNYHIEKR | ---- | ASK  | -KA- | WVS  | -TN | --- | N  | CNRL  | SY  | KVTNLQEG  | --- | AI  | YFRV | SGENEF | --- | VG | IP   | AET    | KEGVKIT   |
| A132_1' | DT | PAAC  | QKLQ | --- | VKHSRGTVTLLWD  | PL | IDGGSP  | IIINYIEKR | ---- | DATK | -RT- | WSV  | -SH | --- | K  | CSST  | SF  | KLIDLSEK  | --- | TP  | FFRV | LAENEY | --- | IG | EP   | CET    | TPVKAA    |
| A143_1' | DT | PGPP  | GPI  | --- | KDVTGRSATLWDA  | PL | IDGGAR  | IHHYVEKR  | ---- | EASR | -KS- | WQVI | -SE | --- | K  | CTRQ  | IF  | KVNDLQEG  | --- | VP  | YFRV | SAVNE  | --- | VG | EP   | YEM    | PEPIVAT   |
| A154_1' | DT | PGPC  | PSVK | --- | VKEVSRDSVTITWE | PT | IDGGAP  | INNYIVEKR | ---- | EAM  | -RA- | FKTV | -TT | --- | K  | SKTL  | YR  | ISGLVEG   | --- | TM  | YFRV | LPENIY | --- | IG | EP   | CET    | SDAVLVS   |
| A58_3'  | GK | PGIPT | GPIK | --- | DEVTAEAMTLKWA  | PP | KDDGGSE | ITNYILEKR | ---- | DSVN | -NK- | WVTC | -AS | --- | A  | VQKT  | TF  | FRVTRLHEG | --- | ME  | YFRV | SAENKY | --- | VG | EP   | GLKS   | EPIVAR    |
| A69_3'  | DI | PGPPT | GPIK | --- | DEVSSDFVTFSWD  | PP | ENDGGVP | ISNYVEMR  | ---- | QDS  | -TT- | WVEL | -AT | --- | T  | VIKT  | TY  | KATRLTTG  | --- | LE  | YFRV | KAQNR  | --- | VG | FP   | GITS   | SAWIVAN   |
| A80_3'  | DK | PGPPT | GPVK | --- | NDEVTADSITLSWG | PP | KYDGGSS | INNYIVEKR | ---- | DST  | -TT- | WQIV | -SA | --- | T  | VART  | TL  | KACRLKTG  | --- | CE  | YFRV | IAENR  | --- | KS | TY   | LNS    | EPTVAQ    |
| A91_3'  | DK | PDPPK | GPVK | --- | FDVSAESITLSWN  | PP | LYTGGCQ | ITNYIQKR  | ---- | DTT  | -TV- | WDV  | -SA | --- | T  | VART  | TL  | KVTKLTG   | --- | TE  | YFRV | IAENR  | --- | QS | FA   | LES    | DPIVAQ    |
| A102_3' | EK | PGPPV | GPVK | --- | DEVSADFVVISWE  | PP | AYTGGCQ | ISNYIVEKR | ---- | DTT  | -TT- | WMV  | -SA | --- | T  | VART  | TL  | KIKLTG    | --- | TE  | YFRV | IAENR  | --- | KS | AP   | LOS    | KAVIVQ    |
| A113_3' | DR | PGPP  | GPIR | --- | DEVSCDSITISWN  | PP | EYDGGCQ | ISNYIVEKR | ---- | ETS  | -TT- | WHIV | -SQ | --- | A  | VART  | SI  | KIVRLTTG  | --- | SE  | YFRV | CAENR  | --- | KS | SS   | SES    | SAVVAE    |
| A124_3' | DR | PGPPT | GPVV | --- | SDITEESVTLKWE  | PP | KYDGGSQ | VTNILLKR  | ---- | ETS  | -AV- | WTEV | -SA | --- | T  | VART  | MM  | KVMKLTG   | --- | EE  | YFRV | IAENR  | --- | IS | DP   | LOS    | ACVTVK    |
| A135_3' | GP | PSKPK | GPVK | --- | DEIKADSVILSWD  | VP | ENDGGGE | ITCYIEKR  | ---- | ETSQ | -TN- | WKM  | -CS | --- | S  | VART  | TF  | KVPNLVKD  | --- | AE  | YFRV | SAENR  | --- | VG | EP   | PLVS   | SIIVAK    |
| A146_3' | GR | PGPVT | GPIE | --- | VSSVSAESCVLSWG | EP | KDGGGT  | ITNYIVEKR | ---- | ESGT | -TA- | WQLV | -NS | --- | S  | VKRT  | Q   | LKTHLTGY  | --- | ME  | YFRV | SAENR  | --- | VS | KLES | APIIAE |           |
| A157_3' | DK | PGPPT | GPIK | --- | DEIDATSITISWE  | PP | ELDGGAP | LSGYVEQR  | ---- | DAHR | -PG- | WLPV | -SE | --- | S  | VTST  | TF  | KFTRLTTEG | --- | NE  | YFRV | LAENR  | --- | IG | SY   | LOS    | EVIECR    |
| A62_3'  | DV | PGPP  | GPVE | --- | ISNVSAEKATLTWT | PP | LDGGSP  | IKSYILEKR | ---- | ETSR | -LL- | WTVV | -SE | --- | D  | IQSC  | RH  | VATKLIQEG | --- | NE  | YFRV | SAVNH  | --- | KG | EP   | LOS    | EPVKMV    |
| A73_3'  | DR | PGPPE | GPIA | --- | DEVTSSEKCVLSWF | PP | LDGGAK  | IDHYIQKR  | ---- | ETSR | -LA- | WTVV | -AS | --- | E  | VQVT  | KL  | VTKLLKG   | --- | NE  | YFRV | MAVNH  | --- | VG | EP   | LOS    | EPVLAV    |
| A84_3'  | DR | PGPPE | GPVV | --- | ISGVTAEKCTLAWK | PP | LQDGGSD | IINYIVERR | ---- | ETSR | -LV- | WTVV | -DA | --- | N  | VQTL  | SL  | CKVTKLLG  | --- | NE  | YFRV | MAVNH  | --- | VG | EP   | LOS    | EPVVAK    |
| A95_3'  | DR | PGPPE | GPVQ | --- | VTGVTSEKCSLWS  | PP | LQDGGSD | ISHYVVEKR | ---- | ETSR | -LA- | WTVV | -AS | --- | E  | VVTNS | L   | KVTKLLG   | --- | NE  | YFRV | MAVNH  | --- | VG | EP   | LOS    | APVLMK    |
| A106_3' | DR | PGSPE | GPIK | --- | VTGVTSEKCTLAWN | PP | LQDGGAN | ISHYIEKR  | ---- | ETSR | -LS- | WTVV | -ST | --- | E  | VQAL  | N   | KVTKLLG   | --- | NE  | YFRV | MAVNH  | --- | IG | EP   | LOS    | GPVTAC    |
| A117_3' | DK | PGPPA | GPIE | --- | INGLTAEKCSLWSG | RP | QDGGAD  | IDYHRRKR  | ---- | ETSH | -LA- | WTIC | -EG | --- | E  | LQMT  | SC  | CKVTKLLG  | --- | NE  | YFRV | TCVNH  | --- | VG | EP   | LOS    | VAIKAL    |
| A128_3' | DK | PGPPG | GPIE | --- | EKVTAEKITLWLR  | PP | ADGGAK  | ITHYIVEKR | ---- | ETSR | -VV- | WSM  | -SE | --- | H  | EECI  | I   | TTKIIKG   | --- | NE  | YFRV | RAVNH  | --- | IG | EP   | LOS    | DSVVAK    |
| A139_3' | DT | PGKVV | GPIR | --- | FNITGEKMTLWDA  | PL | NDGCAP  | ITHYIEKR  | ---- | ETSR | -LA- | WALI | -ED | --- | K  | CEAQ  | SY  | TAIKLING  | --- | NE  | YFRV | SAVNH  | --- | VG | EP   | LOS    | DPVVAQ    |
| A150_3' | DS | PGPC  | GKLT | --- | VSRTQEKCTLWSL  | PQ | DGGAE   | ITHYIVEKR | ---- | ETSR | -LN- | WVIV | -EG | --- | E  | CPTL  | SY  | VVTRLIKN  | --- | NE  | YFRV | RAVNH  | --- | PG | FP   | VES    | EPIVAR    |
| A161_3' | GS | PNSPE | GPIE | --- | YDDIQVRSVRVSWR | PP | ADGGAD  | ILGYILERR | ---- | EVPK | -AA- | WYTI | -DS | --- | R  | VRGT  | SL  | VVKGLKEN  | --- | VE  | YFRV | SAENQF | --- | IS | K    | LP     | KSEEPVTPK |

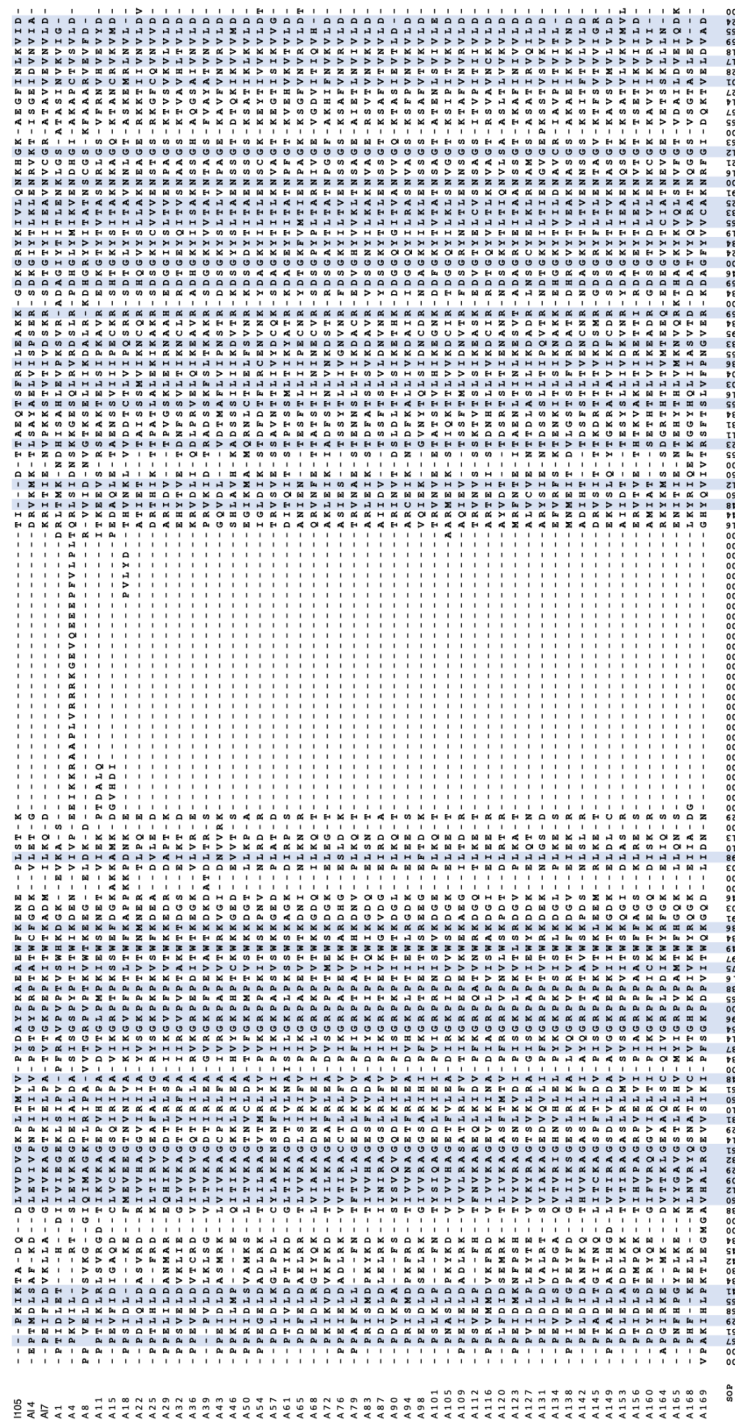
**Type B Subgroups**

|         |              |     |    |               |      |          |            |            |      |      |        |      |     |     |       |      |          |          |     |      |      |      |      |     |     |     |          |            |         |
|---------|--------------|-----|----|---------------|------|----------|------------|------------|------|------|--------|------|-----|-----|-------|------|----------|----------|-----|------|------|------|------|-----|-----|-----|----------|------------|---------|
| A48_4'  | GVPSEP-KNAR  | --- | VT | IVNKDCIFVAND  | RPDS | DGGSP    | IIIGYLERK  | ----       | ERNS | -LL- | WVKA   | -ND  | --- | TL  | VRST  | EYPC | AGLV     | EG       | --- | LEYS | FR   | YALN | KA   | --- | SS  | FP  | SR       | PTEYVTAR   |         |
| A59_4'  | DVPDAP-PPPN  | --- | IV | VNRHDSVSLTWT  | DP   | KKTGGSP  | ITGYHLEFK  | ----       | ERNS | -LL- | WVKA   | -NK  | --- | TP  | IRMR  | DF   | KVTGLT   | EG       | --- | LEY  | FR   | MAIN | LA   | --- | VG  | KP  | SP       | LPSEPVVAL  |         |
| A70_4'  | KVPGGP-GTPQ  | --- | VT | AVTKDSMTISN   | HE   | PLSDGGSP | ILGYHVERK  | ----       | ERNG | -IL- | WQTV   | -SK  | --- | AL  | VPGN  | IF   | KSSGLTDG | ---      | IA  | EYFR | IAEN | MA   | ---  | KS  | KP  | SP  | PEPNLAL  |            |         |
| A81_4'  | KVPGGP-GTPV  | --- | VT | LSRDSMEVQNE   | EP   | ISDGGSR  | VIGYHLEK   | ----       | ERNS | -IL- | WVKA   | -NK  | --- | TP  | IPQT  | K    | FKTGLT   | EG       | --- | VE   | EYFR | SAEN | IV   | --- | IG  | KP  | SP       | SECVVAR    |         |
| A92_4'  | KEPGGP-GTPF  | --- | AT | ISKDSMVIQH    | EP   | VNNGGSP  | VIGYHLEK   | ----       | ERNS | -IL- | WTKV   | -NK  | --- | TI  | HDTQ  | FA   | QNLTEG   | ---      | IE  | EYFR | SAEN | IV   | ---  | VG  | KAS | N   | SECVVAR  |            |         |
| A103_4' | KEPGGP-GTPF  | --- | VT | ISKDQMLVQH    | EP   | VNNGGSP  | VIGYHLEK   | ----       | ERNS | -IL- | WVKL   | -NK  | --- | TP  | IQDT  | K    | FKTGLTDG | ---      | LE  | EYFR | SAEN | IV   | ---  | IG  | KP  | SP  | VSECVVAR |            |         |
| A114_4' | SPFPGP-GTPK  | --- | VV | HATKSTMLVTH   | QV   | VNNGGSP  | VIGYHLEK   | ----       | ERSS | -IL- | WSKA   | -NK  | --- | LI  | ADTQ  | V    | KVSGLD   | EG       | --- | LM   | EYFR | SAEN | IA   | --- | IG  | KP  | SP       | SECVVAR    |         |
| A125_4' | KTPGGP-STPW  | --- | VN | VTRSEITVGH    | EP   | VNNGGSP  | VIGYHLEMK  | ----       | ERNS | -IL- | WOKA   | -NK  | --- | LI  | VRTH  | TK   | VVKTISAG | ---      | LI  | EYFR | SAEN | IA   | ---  | VG  | KP  | SP  | PEPVLA   |            |         |
| A136_4' | RIIPGP-GKPV  | --- | VY | NVTRSGMSTLWDA | PP   | YDGGSE   | ITGYHVEKK  | ----       | ERNS | -IL- | WQKV   | -NT  | --- | S   | PISE  | GE   | TRATGL   | VEG      | --- | LD   | YFRV | SAEN | IA   | --- | LS  | SP  | SP       | KFTLAV     |         |
| A147_4' | VPPSAP-TRPE  | --- | VY | HVSANAMSIRN   | EP   | YDGGSP   | IIIGYHVEKK | ----       | ERNT | -IL- | WVKE   | -NK  | --- | V   | PQLE  | CN   | VKVTGL   | VEG      | --- | LE   | YFRV | TAI  | NA   | --- | VG  | KAS | AS       | SRPMAQ     |         |
| A158_4' | RIIPGP-ETLQ  | --- | ED | VSRDGMTLTW    | YP   | EDDGGSP  | VIGYHVERK  | ----       | EVRA | -DR- | WVRV   | -NK  | --- | V   | PVMT  | YR   | STGLT    | EG       | --- | LEY  | HRV  | TAI  | NA   | --- | SG  | KP  | SP       | SECVVAR    |         |
| A52_4'  | DPPGRC-DPVP  | --- | SN | ITKDHMTVSN    | KP   | ADGGSP   | ITGYLLEK   | ----       | ETQA | -VN- | WTKV   | -NR  | --- | K   | PIERT | L    | KATGLT   | EG       | --- | TE   | EYFR | TAI  | NA   | --- | PG  | KP  | SP       | ASKAAYAR   |         |
| A63_4'  | GPPGGP-EKPE  | --- | VN | VTKNATVSN     | KR   | VDGGSE   | ITGYHVERK  | ----       | EKKS | -LR- | WVRA   | -IK  | --- | TP  | VS    | DLR  | CKVTGL   | EG       | --- | ST   | EYFR | SAEN | IA   | --- | IG  | PP  | SP       | ASDSVLMK   |         |
| A74_4'  | GPPDDP-KNPE  | --- | VT | ITKDSMVVCH    | HP   | DSGGSE   | IIINYIVERR | ----       | EKAG | -QR- | WIKC   | -NK  | --- | KT  | LDLR  | K    | VSGLT    | EG       | --- | HE   | EYFR | MAEN | IA   | --- | IS  | AP  | SP       | SPFYKAC    |         |
| A85_4'  | VVPDAP-KAPE  | --- | VT | VTKDSMVIVH    | ER   | PA       | SDGGSE     | ILGYLLEK   | ---- | EKEG | -IR-   | WTRC | -NK | --- | RL    | IGEL | R        | LVGTGL   | IEN | ---  | HD   | EYFR | SAEN | IA  | --- | LS  | EP       | SP         | SPAYKAC |
| A96_4'  | VLPGGP-KSLE  | --- | VN | TIKDSMTVCH    | NR   | PDGGSE   | IIIGYHVERK | ----       | ERSG | -IR- | WIKC   | -NK  | --- | RR  | ITDL  | R    | LVGTGL   | IEN      | --- | HE   | EYFR | SAEN | IA   | --- | VG  | EP  | SP       | SPATVYKAC  |         |
| A107_4' | KTPGGP-STPE  | --- | VS | AITKDSMVVTH   | AR   | PDGGSE   | IIIGYLERK  | ----       | EKEG | -VR- | WTRC   | -NK  | --- | KT  | LDLR  | K    | LVGTGL   | EG       | --- | HS   | EYFR | SAEN | IA   | --- | VG  | EP  | SP       | SPVFRAC    |         |
| A118_4' | VVPSPG-TSLE  | --- | IS | TVTKESMTLVCH  | SR   | PDGGSE   | IIIGYHIERR | ----       | EKNS | -LR- | WVRV   | -NK  | --- | K   | PVDR  | K    | VSGLT    | EG       | --- | CE   | EYFR | SAEN | IA   | --- | LS  | LP  | SP       | SPPLRAC    |         |
| A129_4' | VTPGGP-GIPE  | --- | VT | KITKNSMTVCH   | NR   | PDGGSE   | IIIGYLERK  | ----       | EKKS | -LG- | WPKV   | -LK  | --- | ET  | IRDR  | K    | VGTGLT   | EG       | --- | SD   | YFRV | CAV  | NA   | --- | Q   | PP  | SP       | SPFYKAA    |         |
| A140_4' | TPVDAP-GIPE  | --- | PS | NITGNSITLTH   | AR   | PDGGSE   | IIIGYLERK  | ----       | EKKS | -TR- | WVKVIS | -R   | --- | P   | ISETR | K    | VGTGLT   | EG       | --- | NE   | EYFR | SAEN | IA   | --- | VG  | PA  | SP       | ISRLIKR    |         |
| A151_4' | TPSPGP-GIPE  | --- | EV | GTGKEHITLQ    | HT   | KP       | SDGGSE     | IIINYIVERR | ---- | EKES | -LR-   | WTRV | -NK | --- | D     | YVYD | TR       | KVTSIMEG | --- | CD   | YFRV | TAV  | NA   | --- | NS  | EP  | SP       | SPSRNEISCR |         |
| A162_4' | NPPEPP-SNPPE | --- | LD | VTKSSVSLWS    | SR   | KDDGGSR  | VIGYHVERK  | ----       | EST  | -DK- | VVRH   | -NK  | --- | TQ  | ITTT  | M    | VTVGLVDP | ---      | AE  | YFRV | IAI  | QNDV | ---  | LS  | EP  | SP  | ASEPVVCK |            |         |

## Type C subgroups

|         |        |          |                                       |         |       |               |                     |                     |           |            |         |
|---------|--------|----------|---------------------------------------|---------|-------|---------------|---------------------|---------------------|-----------|------------|---------|
| A56_2'  | QTPGPV | -VDLK--- | VRSVSKSSCSIGWKKPHSDGGSRIIGYVVDL---    | TEENK   | -D--- | WQRV--MK----  | SLSQYSAKDLTEG--     | KEYTFRVSAENENG--    | EGTP      | SEI--      | TVVAR   |
| A67_2'  | EAPSP  | -DSL---  | IMDITKSTVSLIAWKKPHDGGSKITGYVIEAQ----  | RKGS    | -DQ-- | WTHI--TT----  | VKGLCEVVRNLTG--     | EETTFQVMVNSAG--     | RSAPR     | S--        | RPVIVK- |
| A78_2'  | ERPLPP | -GKIT--- | MDVTRNSVSLSWKKPEHDGGSRIIGYVVEAQ----   | TKGS    | -DK-- | WATC--AT----  | VKTEATITGLIQG--     | EYSFRVSAQNEKG--     | ISDPR     | LSVPVIAK-  |         |
| A89_2'  | EVPQPP | -GKIT--- | DDVTRNSVSLSWTKPEHDGGSRIIGYVVEAQ----   | AKHS    | -EK-- | WSEC--AR----  | VKSLQAVITNLTQG--    | EYLFVRVAVNEKG--     | RSDPR     | LAVPVIAK-  |         |
| A100_2' | EPPSP  | -GKVT--- | LDVSQTSASLMWKKPEHDGGSRIIGYVVEAQ----   | FKGT    | -EK-- | WSIV--AE----  | SKVCNAVVTGLSSG--    | QEQFRVKAYNEKG--     | KSDPR     | VLGVPIAK-  |         |
| A111_2' | EPPLPP | -GRVT--- | LDVTRNTATIKWKKPEHDGGSRIIGYVVEAQ----   | TKGS    | -EK-- | WSC--TQ----   | VKLEATISGLTAG--     | EYVFRVAAVNEKG--     | RSDPR     | QLGVPIAK-  |         |
| A122_2' | EKPSPP | -EKLG--- | VTSISKDSVSLTWLKKPEHDGGSRIIGYVVEAL---- | EKGQ    | -KN-- | WVKC--AV----  | AKSTHHVSVGLREN--    | SEYFRVFAENQAG--     | LSDPR     | LLLPVLIK-  |         |
| A133_2' | EVPAPI | -RDL---  | MKSTKTSVILSWTKPDFDGGSRITGYVVEK----    | GKGE    | -QT-- | WSHA--G----   | GISTCEIEVSQLEKQ--   | SVLEFRVFAKNEKG--    | LSDPR     | VT--       | GPITVK- |
| A144_2' | EQPAPP | -RRLD--- | VDTSKSSAVLWLLKPDHDGGSRIITGYLLEMR----  | QKGS    | -DL-- | WVEA--GH----  | TKQLTFTVERLVEK--    | TEYFRVFAKNDAG--     | YSEPR     | AFSSVIAK-  |         |
| A155_2' | EVPLVP | -AKLE--- | VDDVTKSTVTLWKKPLDGGSRITGYVLEAC----    | KAGT    | -ER-- | WMKV--VT----  | LKPTVLEHTVTSLENG--  | EYLFRIRAQNEKG--     | VSEPR     | TVTAVTVQ-  |         |
| A60_5'  | DPIDPP | -GKPE--- | VINITRNSVTLINTEPKYDGGHKLITGYVIEKR---- | DLP     | -KS-- | WMKA--NH----  | VNVPECAFTVTDLVEG--  | GKYEFRIRAKNTAGAT    | SAPS--    | STETIICK-  |         |
| A71_5'  | DPIDPP | -GKPV--- | PLNITRHTVTLKWKAPYDGGFKITGYVIEKR----   | DLPN    | -GR-- | WLKA--NF----  | SNILENEFTVSGLTED--  | AAYEFRVIAKNAAGAT    | SPPS--    | PSDAITCR-  |         |
| A82_5'  | DPCDPP | -GRPE--- | AIIVTRNSVTLQWKKPTDGGSKITGYVIEKK----   | ELPE    | -GR-- | WMKA--SF----  | TNIIDTHFEVTGLVED--  | HRYEFRVIAKNAAGAT    | SPPS--    | STGATAR-   |         |
| A93_5'  | DPCDPP | -GTPE--- | PIMVKRNEITLQWTKPVYDGGSMITGYVIEKR----  | DLPD    | -GR-- | WMKA--SF----  | TNVIEQTFTVSGLTED--  | QRYEFRVIAKNAAGAT    | SPPS--    | STGATIK-   |         |
| A104_5' | DPCDPP | -GRPE--- | AIIVTRNNVTLKWKAPYDGGSKITGYVIEKK----   | DLPD    | -GR-- | WMKA--SF----  | TNVLETEFTVSGLVED--  | QRYEFRVIAKNAAGAT    | SPPS--    | SSGATIK-   |         |
| A115_5' | DPCDPP | -QQPE--- | VNITRKSISLWKKPHYDGGAKITGYVIEKR----    | ELPD    | -GR-- | WLKC--NY----  | TNIQETTYFTVTELTED-- | QRYEFRVIAKNAAGAT    | SPPS--    | STGPIVIV-  |         |
| A126_5' | DACEPP | -ANVR--- | ITDISKNSVSLWQQAPYDGGSKITGYVIEKR----   | DLPD    | -GR-- | WTKA--SF----  | TNVTEQTFTVSGLTQ--   | SQYEFRVIRANAVISINSE | VVGPICTI- |            |         |
| A137_5' | SPVDPP | -GTPD--- | YIDVTREITITLWKNPPLADGGSKIVGYSIEKR---- | QGN     | -ER-- | WVAC--NF----  | TDVSECQYFTVTSLSQG-- | DRYEFRVIRANAVISINSE | SPPS--    | SSGIMTR-   |         |
| A148_5' | NPVDAP | -GRPE--- | VDDVTRSTVSLIWSAPYDGGSKVVGYYIERK----   | PVSEVGD | -GR-- | WLKC--NY----  | TIVSDNFTVVTALSEG--  | DTYEFRVLAKNAAGAT    | SPPS--    | STGPIVIV-  |         |
| A159_5' | APPGKP | -QNP---  | VDTTTRTSVSLIAWKKPEDEGGSKVTGYLIEMQ---- | KVDQ    | -HE-- | WTKC--NF----  | TEFKIREYTLTLHPQG--  | AEYFRVFLACNAGG--    | EGEFA--   | VPGTVKVT-  |         |
| A64_5'  | YPPGPP | -SNPH--- | VDTTKKSASLWKKPHYDGGLEITGYVVEHQ----    | KVGD    | -EA-- | WIKD--TT----  | GTAIRITQFVVPDLQTK-- | EKYNFRISAINDAG--    | VGEPA     | VIPDVEIVE- |         |
| A75_5'  | FKPGPP | -GNPR--- | VLDTSRSSISIAWKNPIYDGGSEITGYVMEIA----  | LPEE    | -DE-- | WQIV--TP----  | PAGLKATSYTTIGLTEN-- | QYKIRIYAMNSEG--     | LGEPA     | LVPGTPKAE- |         |
| A86_5'  | YKPGPP | -NNPK--- | VIDITRSSVFLWKKPIYDGGCEITGYVIEKC----   | DVNV    | -GE-- | WTMC--TP----  | PTGINKNIEVEKLEK--   | HEYNFRICAINKAG--    | VGEHA     | LVPGPIVIV- |         |
| A97_5'  | YKPGPP | -TNAH--- | IVDTKNSITLWKKPIYDGGSEILGYVVEIC----    | KADE    | -EE-- | WQIV--TP----  | QTGLRVTREISKLEH--   | QYKIRVCAINKAG--     | LGEAT     | LVPGTVKPE- |         |
| A108_5' | YPPGPP | -SNPK--- | VDTSSRSVSLWKKPIYDGGAPVKGYYVEVK----    | EAAA    | -DE-- | WTC--TP----   | PTGLQKQFTVTKIKEN--  | TEYNFRICAINSEG--    | VGEPA     | LVPGSVVAQ- |         |
| A119_5' | FLPSP  | -SKPK--- | IVDSGKTTITLWVKPLDGGAPITGYVVEYK----    | KSD     | -TD-- | WTKS--IQ----  | SLRGTEYTTISGLTIG--  | AEYFRVKSAINKAG--    | ASDPS     | SSDPQIAK-  |         |
| A130_5' | DPPGPP | -AKIR--- | IADSTKSSITLWKKPVYDGGSAVTGYVVEIR----   | QEE     | -EE-- | WTV--STK--G-- | EVRTEYVVSNIKPG--    | VNYFRVSAVNCAG--     | QGEPI     | EMNEPVQAK- |         |
| A141_5' | NPPGPP | -TVVK--- | VDTSKSTVSLIWSKFPYDGGMEILGYVIEIC----   | KDDL    | -GD-- | WHKV--NA----  | EACVKTFTVTDIQAQ--   | EYKFRVSAVNCAG--     | KGDS      | CEVTETKAV- |         |
| A152_5' | YTPGPP | -SAPR--- | VDDTTKKSISLWTKPMYDGGTDIVGYVLEMQ----   | KD      | -DQ-- | WYRV--HT----  | NATIRNTEFTVVDIKMG-- | QYKFRVSAVNCAG--     | MSEYS     | SISAEPEV-  |         |
| A163_5' | DKPSQP | -GELE--- | ILSISKDSVTLQWKKPECDGGKEILGYVVEYR----  | QSGD    | -SA-- | WKS--NK----   | ERIKDKQFTIGGLEA--   | TEYFRVFAENETG--     | LSRPR     | TAMSIKTK-  |         |

**Fig S5. Global MSA alignment of A-band Ig (and I105) domains showing consensus residues.** For each position, the SoP (sum-of-pairs) score is given, where the higher the score the greater the consensus for that alignment position. SoP scores >0.5 and were taken to constitute the global conservation consensus for A-band Igs domains and are marked in pale blue.



**Fig S6: Sequence consensus for Ig domain position within the C-zone super-repeat.** Residues conserved globally and within the A-band Ig are shown in grey. Residues specific to each domain position within the super-repeat (selected according to the criteria of a SoP > 1, at least 90% occupancy of the position and at least 70% sequence identity) are shown in orange.

#### Position i (Ig1)

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A43  --PPEIDLDASHR--KLVIVRAGCPIRLFALV--KGRPAFKVTWRKV--GIDV--VV--RKQVQDLVD--MAFLVIPNSTRD--DSGKYSLTLVVPAGE--KAVFVNVKVLDT--
A54  --PPEGLDADLR--KTLILRAGVTMRLYVP--VXGRPPPKITWSKP--NVNLRDR--IGLDIKSTDF--DFLRCEVNVNY--DAGKYILTLNENSCCK--KEYTIVVKVLDT--
A65  --PPEGLDADLR--KTLVVRAGLSIRIFVP--VXGRPAFEVWTWD--NINLKN---RANIENTES--FTLLIIPCCNRY--DTGKYVMTIENPAGK--KSGFVNVKVLDT--
A76  --PPEGLDADLR--KVVTRACCTLRFLVP--VXGRPAFEVWKARD--HGEILD---KASIENTES--YLLIVGNVNR--DSGKYILTLNENSSGS--KSAFVNVKVLDT--
A87  --PPEIDLDLRL--KVINIRAGGSLRFLVP--VXGRPTFEVWKGV--DGEIRD---AAIIVDTSS--FTSLVDVNVNRY--DSGKYILTLNENSSGS--KSAFVNVKVLDT--
A98  --PELDLDSELR--KGIVVRAGGSARIHIP--VXGRPTFEITWSE--EGEITD---KVQIEKGVN--YTQLSIDNCDRN--DAGKYILTLNENSSGS--KSAFVNVKVLDT--
A109 --PPEGLDADLR--KVVVRAGATLRFLVT--VXGRPEFEVWKKEA--EGILTD---RAQIEVTS--FTMLVIDNVTRF--DSGRVNTLLENSSGS--KSAFVNVKVLDT--
A120 --PELDIDSEMR--KTLIVKAGASFTMTVP--VXGRPVFNVLWSKP--DIDLTR--A--YVDTDS--RTSLTIENANRN--DSGKYILTLIQNVLSA--ASLTLVKVLDT--
A131 --PPEIDLDVALR--TSVIKAGEDVQVLP--VXGRPPFTVTWRKD--EKNLGS--A--ARYSIENTDS--SLLTIPQVTRN--DTGKYILTLIENGVEPKSSTVS--KVLDT--
A142 --PELDIDANFK--QTHVVRAGASIRLFIA--VXGRPTFTAVNSKP--DSNLSLR--A--DHTTDS--FSLTLVENCNRN--DAGKYILTLVENCNRN--KASITFTVLDT--

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#### Position ii (Ig2)

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A46  --P-----KILMP--EQITIKAGKKLRIE--H--VYGGPHPTCKWKK--GEDEVVTSSH--LAVHKADS--SILIIKQVTRK--DSGKYSLTAENSSGS--DTQKIKVVMVD--
A57  --PELDLKLGLPDL--CYLAK--ENSNFRLK--P--IKGKPAFSVSWKKG--EDDPLATD--TRVSVESAV--NTLIVYCCQKS--DAGKYITLKNVAGT--KEGTIS--KVVVG--
A68  --PELDLGLIYQK--LVIAK--AGDNIKVE--P--VLGRPKPTVTWKKG--DQILKQT--ORVNFETAT--STILNINECVRS--DSGKYPLTARNIVGE--VGDVIT--QVH--
A79  --PFAFKLL---FN--TFVL--AGEDLKVDP--V--FGRPTFAVTHKD--NVPIKQT--TRVNAESTEN--NELLTIKQACRE--DVGHVVKLTNSAGE--AIETEL--IVLD--
A90  --PDVKPA---FS--SYSVQ--VGQDLKIE--P--ISGRPKPTITWTKD--GLPKQT--TRINVTDSD--LTLSTIKETHD--DGGQYGITVANVVGQ--KTASIEVT--LD--
A101 --PSLKL---FN--TYSIQ--AGEDLKIE--P--VIGRPFNISWVKD--GEPIKQT--TRVNVETAT--STVLHKKGNKD--DFGKYVTVATNSAGT--ATENLS--IVLE--
A112 --PSVELP---FH--TNVK--AREQLKID--P--FKGRPQATVNRKD--GQTLKET--TRVNVSSKT--VTSLSIKKASKE--DVGTVELCVNSAGS--ITVPIIT--IVLD--
A123 --PEIDMKNFPSH--TVYVR--AGSNLKVDP--V--ISGKPLFKVTLSD--GVPIKAT--MRFNTEITAE--NLTINLKEVTA--DAGRYEITANSSGS--TKAFIN--IVLE--
A134 --PEVDLSIDIPG--AQVTVR--IGHNVHLE--P--YKGRPKPSISNLK--GLPKES--EFVRFSTEN--KITLSIKNAKKE--HGGKYTVILDNAVCR--IAVPIIT--IVLD--
A145 --PTADLTGITNQ--LITCK--AGSPFTID--P--ISGRPAFKVTWKLE--EMRLKET--DRVSIITTKD--RTTLTVKDSMRG--DSGRVYLTLENAGV--KTFSVTV--VIGR--
A156 --PTIDLTSTMPQ--KTIHPV--AGRPVELV--P--IAGRPFAASWFFA--GSKLRES--ERVTVETHTK--VAKLTIR--ETTR--DTGEYTLLELKNVGT--TSETIKV--IILD--

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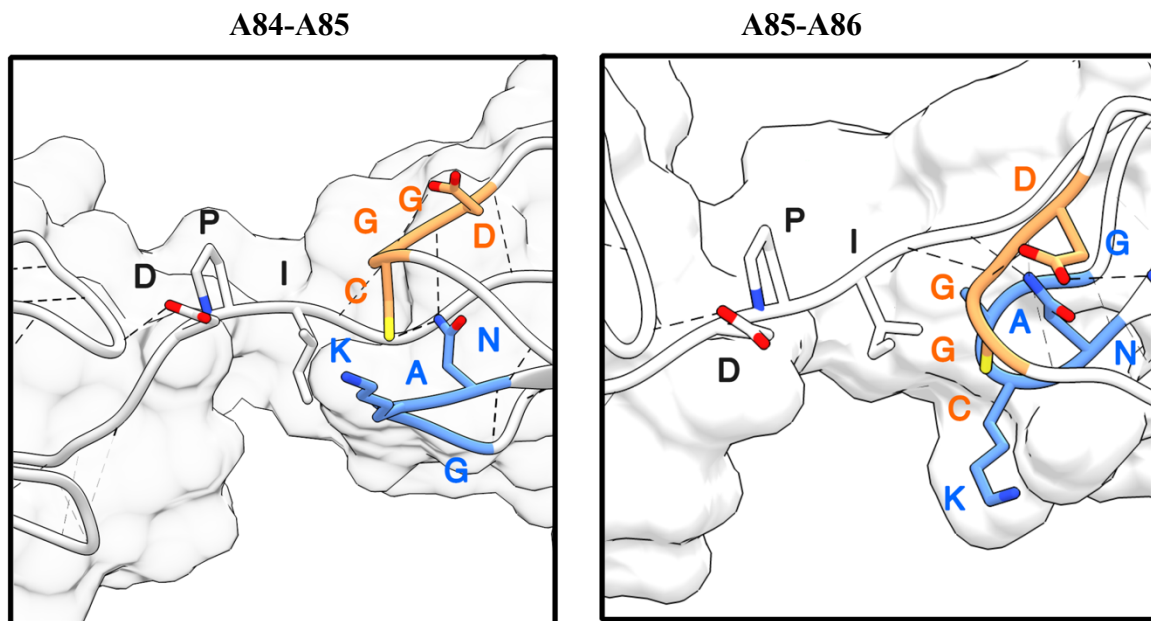
#### Position iii (Ig3)

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A50  --PPEIDLSVAMK--SILTVKAGTNVCLDAT--VFGKPMFTVSNKK--DGLTLKPAEG--IKMAMQRN--LCTLELFSVNRK--DSGKYITTAENSSGS--KSATIKLKVLD--
A61  --PTIVLDPTIK--DGLTIKAGDTIVNLNAISILGKPLKSSNSKA--GKDIRPS--DITQITSTPT--SSMLTIKYATRK--DAGEYITATNPFGT--KVEHVKVTVLD--
A72  --PKIKVDVKFK--DTVILKAGEAFRLEAD--VSGRPPFTMEWSKD--GKLEGT--AKLEIKIADF--STNLVNDSTR--DSGAYITLTATNPGGF--AKHIFNVKVLDT--
A83  --PRISMDPKYK--DTIVVHAGESFKVDAD--YIGKPIFTIQWIKG--DQELSN--ARLEIKSTDF--ATSLSVKQAVRV--DSGNYILKAKNVAGE--RSVTVNVKVLDT--
A94  --PRISMDPKYK--DTIVVHAGETFRLEAD--VHGKPLFTIEWLRG--DKEEES--ARCEIKNTDF--KALLIVKQAIRI--DGGQYILRASVAGS--KSPFVNVKVLDT--
A105 --PFAELDPKFK--DIVVHAGETFFLEAD--IRGKPIFDVWMSKD--GKLEETA--ARMEIKSTIQ--KETLVVVCICIT--DGGQYILKLSVGGT--KSIFITVKVLDT--
A116 --PRVMMMDVKFR--DIVVVRAGETVLKINAD--IAGRPLFVTSWAKD--GIEER--ARTEIISTDN--HELLTVKOCIR--DTGQYVLTLLKVA--TSVAVNVKVLDT--
A127 --FVIDLPLEMT--EIVVKYRAGESVKLRAG--ISGRPAFTIEWKD--DKLEQTN--ALVCEVNTD--LASILKQADRL--WSGKYELRLNAMS--ASATIRVQILD--
A138 --PPIVEGPEVF--DLIIRSGESLRIKAL--VQGRPVFRVTFD--GVLEKR--MNMETDVLG--STSLFVQATRD--HRCVTVVAKKASGS--AKAEIKVQVND--
A149 --PFAELDARLHG--DLVTRAGSDVLVDAA--VGGKPEFKITWTKG--DKE--DLIC--EKVSLQYTGK--RATAVIKFCDS--DSGKYITLVKNASGT--KAVFVNVKVLDT--

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**Fig S7: Domain interfaces in the extended conformation of the remaining copy of A84-A86 in the crystal structure**



**Fig S8: Residue composition of patches of positionally conserved surface residues**

A. Conservation of residues in the first Ig of super-repeats C2-C11 displayed for the domain in C4; **B.** As A. but for FnIII in position 7 of the super-repeat displayed on domain A82.

